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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 102008

Application Number: 08/870,762
Filing Date: 06/06/1997
Appellant: Duft *et al.*

For Appellant
Steven C. Koerber

EXAMINER'S ANSWER

This is in response to Appellant's brief on appeal filed 08/07/2008.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The Examiner is aware of a related pending appeal in application 09/445,517, which is a continuation-in-part of the instant application, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement on the status of the claims contained in the brief is correct.

This appeal involves claims 1-7 and 9-17.

Claim 8 was previously canceled.

(4) Status of Amendment After-Final

The Appellant's statement of the status of after-final amendment contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of the claimed subject matter contained in the appeal brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The Appellants' statement of the grounds of rejection to be reviewed on appeal is correct.

Withdrawn Rejection(s)

(i) The following ground of rejection is not presented for review on appeal because the rejection has been withdrawn upon further consideration and/or based on Appellants' arguments presented in the appeal brief.

The rejection of claims 3 and 17 made in paragraph 29 of the Office Action mailed 02/11/08 and maintained in paragraph 14 of the Office Action mailed 04/30/08 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the full scope, is withdrawn.

(ii) The as-evidenced-by reference of Rink *et al.* (US 5,739,106) ('106) cited in the rejection of claims 7, 14 and 16 made under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 13 of US patent 5,321,008 issued to Beumont *et al.* ('008) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract) has been withdrawn. The rejection however is maintained.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

The following evidence is relied upon by the Office in the rejection of the claims under appeal.

1) US patent 5,686,411 ('411) issued to Gaeta *et al.* and published 11/11/1997
2) Tsanev A. *Vutr. Boles*. 23: 12-17, 1994, abstract
3) US patent 5,321,008 ('008) issued to Beumont *et al.* and published 06/14/1994
4) US patent 5,739,106 ('106) issued to Rink *et al.* and published 04/14/1998
5) WO 92/20367 of Rink *et al.*, published 11/26/1992
6) US patent 5,364,841 ('841) issued to Cooper *et al.*, published 11/15/1994
7) US patent 5,280,014 ('014) issued to Cooper *et al.*, published 01/18/1994
8) Rattner *et al. Exp. Clin. Endocrinol. Diabetes* 113: 199-204, 2005 (Rattner, 2005)

9) Baron *et al. Current Drug Targets – Immune, Endocrine & Metabolic Disorders* 2: 63-82, 2002

10) US patent 5,175,145 ('145) issued to Cooper *et al.*, published 12/29/1992

11) WO 96/40220 ('220) of Kolterman *et al.*, published 12/19/1996

12) Kolterman *et al. Diabetologia* 39: 492-499, 1996 (Kolterman *et al.,* 1996)

13) Itasaka *et al. Psychiatr. Clin. Neurosci.* 54 : 340-341, 2000

14) Thompson *et al. Diabetes* 46: Suppl. 1, page 30A, 0116, May 02, 1997

15) Ratner *et al. Diabetes Technol. Ther.* 4 : 51-61, 2002

(9) Grounds of Rejections

The following grounds of rejections are applicable to the appealed claims.

Rejection(s) under 35 U.S.C § 112, First Paragraph (Scope of Enablement)

(A) Claims 1, 2, 4-7 and 9-16 are rejected under 35 U.S.C § 112, first paragraph, because the specification, while being enabling for a method of reducing the body weight of an insulin-taking type 2 diabetic human subject having a body weight not varying more than 45% from the desirable weight, by subcutaneous administration to said subject, an amount of the amylin agonist analogue species, ^{25,28,29}Pro-h-amylin (SEQ ID NO: 1), i.e., pramlintide, wherein said pramlintide is not in conjunction with another obesity relief agent, and wherein said amount of the pramlintide significantly reduces the mean body weight of said human subjects after four weeks of said treatment compared to the mean body weight of said subject prior to said treatment, does not reasonably provide enablement for a method of treating obesity in any human subject including a non-diabetic human subject in need of treatment for obesity, or a diabetic human subject in need of treatment for obesity who is not on insulin therapy, comprising or consisting of administering a generic amylin, a generic amylin agonist other than calcitonin or CGRP, or any amylin agonist analogue other than pramlintide (SEQ ID NO: 1), as claimed in a broad sense. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

Instant claims are evaluated based on *Wands* factors. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability in the art; and
- The breadth of the claims.

In the instant application, the nature of the invention is pertinent to the treatment of obesity in a human subject in need of such treatment comprising or consisting of administering an amylin, an amylin agonist, or an amylin agonist analogue composition or compound in an amount effective to inhibit weight gain or induce weight loss in said subject. As described in the instant specification, the state of the art recognizes obesity or adiposity to be a 'chronic disease' that is highly prevalent in modern society which is strongly associated with multiple conditions including diabetes mellitus, insulin resistance, hypertension etc. The limitation 'obesity' encompasses diabetes-associated obesity, non-diabetes-associated obesity, morbid obesity, aging-associated obesity, insulin requiring obesity, obesity associated with family genetics, obesity due to hypernutrition etc. With regard to the breadth, the method claimed in claims 1, 2, 4, 5, 7 and 14-16 does not require that a specific amount of the recited amylin or amylin agonist be administered, whereas the method of claims 6 and 9-13 recite specific amounts of amylin or amylin agonist be administered. The method of claims 1, 2, 5, 7 and 13-16 does not require that the recited amylin or amylin agonist be administered via a specific route, whereas claim 4 recites that the administration is by subcutaneous route. Claims 1, 2, 14 and 16 encompass administration of any amylin or amylin agonist by any route, in any quantity, and any number of times per day, to any human subject in need of treatment for obesity for any length of time.

The step recited in claim 1 'consists of administering' to said human subject, an amount effective to inhibit weight gain (i.e., maintain the existing weight) or an amount effective to induce weight loss in said human subject, of a composition 'comprising' a pharmaceutically acceptable carrier and an amylin or an amylin agonist. Such an administration step *excludes* administration of any other substance, simultaneous insulin administration, or insulin administration before or after the administration of an amylin, amylin agonist, or an amylin agonist analogue. Furthermore, because of the open claim language 'comprising', the composition recited in claims 1 and 2 is

allowed to comprise one or more obesity relief agents, or any other compounds in addition to amylin or an amylin agonist. As claimed currently, 'an amount effective to inhibit weight gain or induce weight loss in said human subject' is not the amount of the recited amylin or the amylin agonist, but of the composition that 'comprises' an amylin, amylin agonist, or an amylin agonist analogue plus a pharmaceutically acceptable carrier plus any other element that is 'comprised' within the composition, including another anti-obesity agent. 'Therapeutically effective amounts' of an amylin, an amylin agonist, or an amylin agonist analogue, for use in the control of obesity are described in the specification as 'those that decrease body weight', but are not described as amounts that inhibit weight gain, i.e., an amount that maintains the weight as existed prior to the treatment. See last full sentence on page 22 of the instant specification. The method of treating obesity in a human subject in need of treatment for obesity as claimed in the independent claim 7 'comprises' administering to said subject an amount of a composition comprising a pharmaceutically acceptable carrier and an obesity relief agent 'consisting' of an amylin or an amylin agonist in an amount effective to inhibit weight gain or induce weight loss in said human subject and is effective to treat obesity. The method of treating obesity in a human subject in need of treatment for obesity as claimed in the independent claim 14 'comprises' administering to said subject a compound selected from the group consisting of an amylin, an amylin agonist, and salts thereof, wherein the compound, including the salt compound, is administered in an amount effective to treat obesity by inhibiting weight gain or inducing weight loss, and wherein said compound is not administered in conjunction with another obesity relief agent. The method of treating obesity in a human subject in need thereof as claimed in the independent claim 16 'comprises' administering to said subject an effective amount of a 'composition consisting essentially of an amylin or an amylin agonist, wherein said amount' of the composition is effective to treat obesity by inhibiting weight gain or inducing weight loss in said subject. The instant disclosure lacks a specific definition for the limitation 'a composition consisting essentially of an amylin or an amylin agonist' as to what it excludes or includes, and therefore one cannot envisage whether or not the composition includes or excludes an element such as insulin, glucagon, an anti-diabetic agent, or a gastric emptying agent etc. The limitation 'a human subject … in need of treatment for obesity' encompasses an overweight, moderately obese, morbidly obese, diabetic and non-diabetic obese, insulin-requiring and insulin non-requiring obese human subject as well as a

human subject with natural aging-associated obesity. The limitations 'amylin agonist' and 'amylin agonist analogue' broadly encompass a myriad of compounds, including a peptide and a nonpeptide compound (see paragraph bridging pages 13 and 14 of the original specification), non-human amylins, amylins having amino acid modifications or substitutions, variants of amylin, and the art-accepted amylin agonists such as calcitonin and CGRP (see lines 45-47 in column 7 of US patent 5,739,106 and claims 3 and 10 of US 5,175,145) etc.

With regard to scope of enablement, a review of the instant specification indicates that Examples 2-4 and 9-20 are not enabling of the claimed method of treatment. Instead, these Examples describe how to prepare selective amylin agonist analogues. Example 5 pertains to the evaluation of *in vitro* binding of compounds to amylin receptors whereas Example 6 pertains to the determination of amylin agonist activity of the compounds as measured by soleus muscle assay. Examples 7 and 8 describe methods of measuring gastric emptying using phenol red and tritiated glucose gastric emptying assays. What are claimed however are not amylin agonist analogues, or a method of making them, or using them in *in vitro* assays as described in Examples 2-4 and 9-20 of the instant specification, but a method of treating obesity in a mammal in need of treatment for obesity by administering *in vivo* a weight gain-inhibiting effective amount or a weight loss-inducing effective amount of an amylin, amylin agonist, or amylin agonist analogue. Example 1 of the instant specification indicates that the human subjects used in the instant invention are those with a history of type 2 diabetes mellitus, who *required* insulin treatment for at least 6 months prior to the pre-screening visit. Body weight-wise, i.e., obesity-wise, these patients are described as having a body weight not varying more than 45% from the 'desirable weight' before admission into the study based upon Metropolitan Life Tables. The only amylin agonist species or amylin agonist analogue species that was administered to these type 2 diabetic patients was ^{25,28,29}Pro-h-amylin (SEQ ID NO: 1), also known as pramlintide. Groups of patients were given separate mealtime pramlintide, 30 micrograms QID; 60 micrograms QID, or 60 micrograms TID subcutaneously before 15 minutes of each meal three to four times a day. Patients *remained on their insulin, usual diet, and exercise regimens* and therefore the method 'comprised' administration of pramlintide as explained above, along with the administration of insulin. The study period was limited to four weeks, i.e., 28 days, and the outcome was determined by comparing, at the end of four weeks, the mean body weight of the

treated diabetic subjects with the mean body weight of the subject prior to the treatment. Thus, the originally filed specification at pages 30-31 and Table I describes a *statistically significant reduction* in the mean baseline weight seen after the subcutaneous administration of 60 micrograms TID or 60 micrograms QID of one specific amylin agonist species or amylin agonist analogue species, pramlintide (SEQ ID NO: 1), to type 2 diabetic subjects for four weeks, wherein said pramlintide administration was *accompanied* with the continued use of insulin. The method as described in the originally filed specification thus comprised insulin treatment *and* the administration of a specific dose of pramlintide in type 2 diabetic patients via a specific route. The decrease in body weight observed was statistically significant compared to the body weight of those type 2 diabetes patients who were treated with insulin alone. However, this single enabled embodiment is not representative of the full scope of the claims which broadly encompasses the administration of any amylin, any amylin agonist, or any of a plethora of non-pramlintide amylin agonist analogues in the treatment of obesity in diabetic and non-diabetic patients *not* on insulin treatment. While there is no requirement for Applicants to enable all of the amylin species, amylin agonist species, or amylin agonist analogue species encompassed within the claimed invention, enablement of a reasonable or representative number such species in the claimed method is required. This is critically important because at the time of the invention, there was no predictability that if one used an amylin, amylin agonist, or a non-pramlintide amylin agonist analogue in place of Applicants' pramlintide (SEQ ID NO: 1) in type 2 diabetic or non-diabetic overweight or obese subjects who are on or not on insulin treatment, or in morbidly obese human subjects who are on or not on insulin therapy, the administered amylin, amylin agonist, or non-pramlintide amylin agonist analogue would bring about significant or clinically meaningful weight loss-inducing, weight gain-inhibiting, or obesity-relieving effect. Neither the state of the art *at the time of the invention*, nor the instant specification as originally filed, provides specific guidance and direction with regard to the use of a generic amylin, or a non-pramlintide or non-calcitonin amylin agonist, or a non-pramlintide amylin agonist analogue to treat obesity in a generic human subject in need of treatment for obesity.

Upon consideration of the evidence as a whole and analysis of all of the *Wands* factors, the instantly claimed methods are viewed as being non-enabled with regard to the full scope. It should be noted that the scope of the required enablement varies inversely with the degree of

predictability involved. A single embodiment may provide broad enablement in cases involving predictable factors. However, in applications directed to inventions in arts where results are unpredictable, the disclosure of a single species does not provide an adequate basis to enable generic claims. MPEP § 2164.03. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. In the instant case, it is not obvious from the disclosure of the administration of pramlintide species in the treatment of obesity in type 2 diabetic humans, what other amylin species, non-pramlintide species, or salts thereof would work in treating obesity in diabetic or non-diabetic humans in need of treatment of obesity, with or without co-administration of insulin. It should be noted that predictability or unpredictability is one of the *Wands* factors to be considered for enablement or lack thereof under 35 U.S.C § 112, first paragraph. The instantly claimed invention is in an area of art that is unpredictable. Amylin, a sufficient number of non-pramlintide amylin agonist analogues, and salts thereof, are not enabled as obesity relief agents in the instantly claimed method. Mere recitation of representative examples of amylins, amylin agonists, or amylin agonist analogues of the claimed genus together with a statement applicable to the genus as a whole is not sufficient to enable the full scope of the claimed methods, because one skilled in the art would not expect that the claimed genus could be used in that manner without undue experimentation. A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, *unless* there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971).

In the instant case, one of the reasons for doubting the objective truth of the statements comes from Appellants' own statement. For example, Appellants have readily acknowledged previously that administration of amylin would have lead to *weight gain* rather than *weight decrease* as was known at the time of the invention via the disclosure of US patents 5,364,841 and 5,280,014. Applicants have expressly stated previously that at the time of the invention, amylin was administered to patients suffering from *anorexia* or *a similar condition* 'in order to increase weight'. See pages 7 and 8 of Appellants' amendment filed 03/22/99. Thus, at the time of the invention, amylin at a dose varying from about 0.1 to 10 mg (which dose encompasses the doses recited in the instant claims, including claims 6 and 9-13) was administered to treat patients suffering from *anorexia* or *patients deficient in adipose tissue*. See also claims and page 13 of Rink *et al*. (WO 9220367). This alone is *prima facie* evidence for the lack of scope of enablement of the instantly claimed method of treating obesity as claimed comprising administration of amylin as claimed. Therefore, despite the level of skill in the art and despite the structural relatedness to pramlintide, there is no predictability that administration of a dose of amylin varying from about 0.1 to 10 mg to a human patient in need of treatment for obesity would have resulted in inhibition of weight gain or induction of weight loss. Instead, one of skill in the art would have expected induction of weight gain upon administration of amylin as acknowledged by Appellants. With the weight gain-increasing effect of amylin known at the time of the invention, one of skill in the art would have reasonably expected amylin and the innumerable number of non-pramlintide amylin agonists or amylin agonist analogues encompassed within the scope of the instant claims, to be therapeutic for anorexia. The administration of amylin or a non-pramlintide amylin agonist analogue would *not* have predictably brought about weight gain-inhibiting or weight loss-inducing effect. Thus, in view of level of skill, the state of the art at the time of the invention, and the information in the specification, one of skill would *not* expect that the recited genus could be used in that manner without undue experimentation. Therefore, the considerable amount of experimentation needed in the instant case is not merely routine, but undue in view of the unpredictability and the lack of evidence enabling the full scope of the invention.

Furthermore, with regard to the state of the art at the time of the invention, Appellants have previously gone on the record with the following (see pages 9, 13 and 14 of Appellants' Appeal Brief filed July 2000) [Emphasis in original]:

> .... THE RINK PATENT PROVIDES THAT AMYLIN AND AMYLIN AGONISTS ADMINISTERED AS DESCRIBED AND CLAIMED IN THE PRESENT APPLICATION HAVE "NO MEASURABLE EFFECT" ON FOOD INTAKE.
>
> .... the Rink patent reports that a 1.0 μg/kg dose (**equivalent to about 70μg/dose in an adult human**) had no effect on food intake. [Emphasis in bold added]

The Rink patent that is being referred to *supra* by Appellants is US 5,739,106. Note that the above-mentioned about 70 μg/dose in an adult human is encompassed within the therapeutic amount range of about 0.01 to about 5 mg, or about 0.05 to about 2 mg of amylin, as recited in instant claims 12-14. Thus, in view of the above-cited acknowledgment of the failure of amylin to have any effect on food intake, one of skill in the art would look into Appellants' specification for specific guidance and direction for the use of amylin in treatment of obesity. However, the instant specification fails to show that human or non-human amylin or a salt thereof, or a composition comprising, consisting of, or consisting essentially of the same, was in fact stable, soluble and/or non-aggregating enough to be 'therapeutic' in a method of treating obesity upon administration in any amount and by any route, with or without concurrent insulin therapy, to a diabetic or non-diabetic human subject in need of treatment for obesity. This is important because with regard to the therapeutic use of amylin, the state of the art indicates difficulty, undesirable pharmacological properties, and impracticability of using amylin, including human amylin, clinically as 'a therapeutic agent'. For instance, Baron *et al.* (*Current Drug Targets – Immune, Endocrine & Metabolic Disorders* 2: 63-82, 2002) taught the following with regard to the clinical use of amylin as a therapeutic agent:

> Clinical use of amylin as a therapeutic agent is considered impractical because of its instability in solution and its propensity to aggregate and adhere to surfaces, properties that hamper the manufacturing, formulation, and storage of this peptide as a drug. Pramlintide is a synthetic, equipotent analogue of human amylin in which the undesirable pharmacological properties of human amylin (insolubility, tendency to self-aggregate) have been overcome by replacement of the three amino acid residues .... with prolines ....

Ratner *et al.* (*Diabetes Technol. Ther.* 4: 51-61, 2002) provide a similar teaching (see paragraph bridging the two columns on page 52):

> Native human amylin is not ideal for clinical use because of the peptide's poor solubility and propensity to aggregate.

Thus, for the reasons delineated above and due to the lack of specific direction or guidance within the instant specification, the breadth of the claims, the absence of working examples enabling the full scope, the art-recognized unpredictability factor, and the quantity of the experimentation necessary, a considerable amount of non-routine undue experimentation would have been required to reproducibly practice the full scope of the invention, as claimed. Instant claims do not meet the scope of enablement provisions of 35 U.S.C. § 112, first paragraph.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

(B) Claims 1, 7, 14 and 16 and the dependent claims 2-6, 9-13, 15 and 17 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1 and 7, as amended, include the new limitations: 'an amount effective to inhibit weight gain or induce weight loss … of a composition comprising an amylin or amylin agonist …… wherein said subject is in need of treatment of obesity'. Claim 16, as amended, includes the new limitations: an amount 'effective to inhibit weight gain or induce weight loss … of a composition consisting essentially of an amylin or amylin agonist …… said subject is in need of treatment of obesity'. Claim 14, as amended, includes the new limitation: 'salts thereof ….. in an amount effective to treat obesity 'in said subject by inhibiting weight gain or inducing weight loss wherein said subject is in need of treatment for obesity'. As claimed currently, 'an amount effective to inhibit weight gain or induce weight loss in said human subject' is not the amount of the recited amylin or the amylin agonist, but of the composition that 'comprises' therein an amylin, amylin agonist, or an amylin agonist analogue plus a pharmaceutically acceptable carrier plus any other element that is comprised within the composition. Applicants state that the amendment to claims 1, 7, 14 and 16 find support at page 9, lines 9-11 and 15-16, and page 22, lines 27-28 of the specification. However, lines 9-11 and 15-16 of page 9 of the specification are not supportive of 'an amount effective to inhibit weight gain ……. in said human subject …..' or 'an amount of a

composition comprising a pharmaceutically acceptable carrier and an amylin or an amylin agonist effective to inhibit weight gain or induce weight loss in said human subject'. The description at lines 27 and 28 of page 22 of the specification is limited to therapeutically effective amounts of amylin or amylin agonist analogue for use in the control of obesity, which are described as those that *decrease body weight*. An 'amount effective to inhibit weight gain' is an amount effective in maintaining the body weight as it existed prior to the treatment, for which there is no support. The specification does not support the new limitation of an amount of an amylin or an amylin agonist 'effective to inhibit weight gain' in a human subject in need of treatment for obesity, or 'an amount of a composition comprising a pharmaceutically acceptable carrier and an amylin or an amylin agonist effective to inhibit weight gain or induce weight loss in said human subject'. The limitation 'composition comprising' in the instant claim(s) does not exclude additional, unrecited elements. See MPEP 2111.03 [R-1]. See *Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986)*; *In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ('comprising' leaves 'the claim open for the inclusion of unspecified ingredients even in major amounts') [Emphasis added]. Instead, the limitation 'comprising' allows the inclusion of additional anti-obesity agents such as exendin, CCK etc., as well as elements such as insulin or glucagon, to be present in the recited composition. Therefore, an amount of a composition 'comprising' amylin or amylin agonist would include an amount of exendin, CCK, or insulin etc. There is no descriptive support for 'an amount of a composition comprising an amylin or amylin agonist' said 'amount effective to inhibit weight gain or weight loss' in said human subject. Instead, what is supported in Example 1 and Table I is an amount of the amylin agonist analogue pramlintide (e.g., 60 micrograms QID or TID) that is effective to decrease body weight.

Additionally, there is lack of descriptive support for an amount of a 'salt' of amylin or an amylin agonist compound and its administration to a human subject in need of treatment for obesity wherein the amount of the salt is effective to treat obesity in said subject by inhibiting weight gain or inducing weight loss, wherein the salt compound is not administered in conjunction with another obesity relief agent, as claimed currently in the amended claim 14.

Furthermore, the amended claim 1 continues to include the limitation: 'method of treating obesity …. consisting of administering …. an amount effective to inhibit weight gain or induce weight loss …… of composition comprising an amylin or an amylin agonist and a pharmaceutically acceptable carrier'. A method of treatment of obesity 'consisting of' such an administration step *excludes,* for example, simultaneous insulin administration, or insulin administration minutes or hours before or after the administration. However, neither the original six claims, nor the description of the methods of treatment of the instant invention support such a method of treating obesity 'consisting of' administering an effective …… composition comprising an amylin or an amylin agonist and a pharmaceutically acceptable carrier. For example, the originally filed specification at lines 6-8 of page 9 of the specification states [Emphasis added]:

> The present invention is directed to novel methods for treating or preventing obesity in humans *comprising* the administration of an amylin or an amylin agonist, the amylin agonist analogue ^{25,28,29}Pro-human amylin.

Pages 30-31 and Table I of the specification describe a statistically significant reduction in the mean baseline weight seen after the subcutaneous administration of 60 micrograms TID or 60 micrograms QID of one specific amylin agonist analogue species, pramlintide, to type II diabetic subjects for four weeks, wherein said pramlintide administration was accompanied *with the continued administration of insulin*. Thus, the method of treatment of obesity as described in the originally filed specification *comprised* insulin administration *and* the administration of a specific dose of pramlintide to type II diabetic patients. This however does not provide descriptive support for the now claimed method of treating obesity in a human in need of treatment for obesity, said method 'consisting' of administering to said subject an amount of a composition as recited comprising an amylin or any amylin agonist and a pharmaceutically acceptable carrier, wherein said amount of the composition is effective to inhibit weight gain or induce weight loss in said subject. Therefore, the above-identified limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P. 608.04 to 608.04(c). Applicants are to specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

(C) Claims 1-7, 9-14, 16 and 17 are rejected under 35 U.S.C § 102(a) as being anticipated by Kolterman *et al.* (WO 96/40220) ('220) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract).

Kolterman *et al.* ('220) taught a method of administering to insulin-taking type II diabetic human subjects a dose of 10, 30, 50, 60 or 150 micrograms per day (i.e., the amount falling in the range recited in the instant claims) of the amylin agonist composition, pramlintide or $^{25, 28, 29}$pro-h-amylin, also known as AC137 (i.e., SEQ ID NO: 1), i.e., the same amylin agonist administered in the instantly claimed method. The composition consists of pramlintide and a pharmaceutically acceptable carrier, and is administered in single or multiple doses, for example, of about 30 micrograms QID, or about 60 micrograms TID or QID, i.e., an amount effective to inhibit weight gain or induce weight loss. See pages 9-11; paragraph bridging pages 20 and 21; page 21; first paragraph on page 19; lines 8-10 on page 19; and the first row reciting 'Insulin-Treated Patients' in each Table of Kolterman *et al.* ('220). Pramlintide is administered subcutaneously 1-4 times a day, before meals. See pages 9 and 22. Kolterman *et al.* ('220) additionally taught that the presence of obesity is a characteristic of 'most patients with Type II diabetes mellitus'. See page 10. Kolterman *et al.* ('220) taught the benefit of obtaining weight loss in Type II diabetic patients by teaching that hyperglycemia associated with Type II diabetes can be reversed or ameliorated by *weight loss* sufficient to restore the sensitivity of the peripheral tissues to insulin (see pages 7, first paragraph), thus teaching that Type II diabetic patients are indeed in need of weight loss or treatment of obesity. Thus, the very active step of the instantly claimed method was disclosed and practiced by Kolterman *et al.* ('220) in 1996 in the very same patient population, i.e., a human type II diabetes mellitus patients used by Applicants in Example 1 of the instant application. The prior art method is the *same* as the instantly claimed method with regard to

the amylin agonist or the amylin agonist analogue, the amylin agonist composition, or the amylin agonist analogue composition (pramlintide) administered, and the insulin-taking Type II diabetic patients used (80-90% of Type II diabetic patients being known in the art to be intrinsically obese as taught by Tsanev - see Tsanev's abstract), the subcutaneous route of the administration used, the dose and the daily frequency of the amylin agonist pramlintide administered, and the administration step prior to meals. Given Tsanev's express disclosure that 80 to 90% of type II diabetic patients are intrinsically obese, and given Kolterman's ('220) recognition that obesity is an intrinsic characteristic of most patients with Type II diabetes mellitus and the indication that these patients are in need of weight loss, Kolterman's ('220) method of subcutaneous administration of pramlintide to Type II diabetic patients in an amount that falls within the range recited in the instant claims, necessarily serves as the claimed method of treating obesity, and therefore anticipates the instantly claimed method. Since 80-90% of Type II diabetic patients are known in the art to be intrinsically obese, 80-90% of Kolterman's ('220) type II diabetic patients to whom pramlintide composition is administered, necessarily qualify as human subjects in need of treatment of obesity as recited in the instant claims. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the teachings of Kolterman *et al.* ('220), Kolterman's ('220) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain inhibiting effect, or weight loss-inducing effect. The Office's position that Kolterman's ('220) method is the same as the Applicants' claimed method is based upon the fact that the method step, the pramlintide compound administered, the amount of the compound administered, the route by which the compound is administered, and the intrinsically obese diabetic human patients to which the pramlintide compound is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see Tsanev's abstract), Kolterman's ('220) method of administration of the above-identified therapeutically effective amount (i.e., about 30 micrograms QID, or about 60 micrograms TID or QID, or a dose of 10, 30, 50, 60 or 150 micrograms per day) of the amylin agonist ^{25,28,29}Pro-human amylin to intrinsically obese type 2 diabetic human subject species anticipates the instant claims. Given that the method step of the Kolterman's ('220) method and the instant claims are the same, Kolterman's ('220) method is expected to bring about weight gain-inhibiting or weight loss-causing therapeutic effect in the intrinsically obese pramlintide-treated type II diabetic patients. Since the prior art clearly

teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist pramlintide in the claimed method are merely inherent and do not necessarily make the claimed method patentable. The art-recognized intrinsic obesity being prevalent in as much as 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Kolterman's ('220) method of administration of the above-identified therapeutically effective amount (i.e., about 30 micrograms QID, or about 60 micrograms TID or QID, or a dose of 10, 30, 50, 60 or 150 micrograms per day) of the amylin agonist ^{25,28,29}Pro-human amylin to intrinsically obese type 2 diabetic human subject species anticipates the instant claims.

Claims 1-7, 9-14, 16 and 17 are anticipated by Kolterman *et al.* ('220). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Kolterman *et al.* ('220), but rather is used to show that every element of the claimed subject matter is disclosed by Kolterman *et al.* ('220), with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., 80 to 90% prevalence of obesity in Kolterman's ('220) diabetic subjects administered with pramlintide, is necessarily present in the method thing described by Kolterman *et al.* ('220). The method of Kolterman *et al.* ('220) clearly anticipates the claimed method of the instant invention, because Kolterman *et al.* ('220) taught the very step of the instantly claimed method in the very same type II diabetic human patient population. Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the disclosure of Kolterman *et al.* ('220), Kolterman's ('220) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the weight gain-inhibiting effect, weight loss-inducing effect, or obesity-treating effect.

(D) Claims 1-7, 9, 11-14, 16 and 17 are rejected under 35 U.S.C § 102(b) as being anticipated by Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996) (Kolterman *et al.*, 1996) as evidenced by Itasaka *et al.* (*Psychiatr. Clin. Neurosci.* 54: 340-341, June 2000).

It is noted that the human patient in need of the recited treatment according to the instant invention is expressly identified in the instant specification as one having a body weight of 79 kg. A 70 kg patient is not excluded from the scope of the instant invention 'as a human subject in need thereof', but is expressly included. The recited therapeutic amount range of 'about 0.1 milligrams per day to

about 1 milligram per day', or 'about 0.01 to about 5 mg/day', or 0.03 to about 5 mg/day of the amylin agonist or amylin agonist analogue, pramlintide, administered is specifically "for a 70 kg patient". See lines 4-8 of page 23 of the substitute specification; and paragraph bridging pages 23 and 24 and lines 3-7 on page 24 of Applicants' response filed December 2002.

Kolterman *et al.* (1996) taught a method of subcutaneous administration of 30, 100, or 300 μg of pramlintide composition or AC137 (i.e., $^{25, 28, 29}$pro-h-amylin or SEQ ID NO: 1), a human amylin analogue, to human patients with insulin-dependent diabetes mellitus or IDDM who are on insulin. Pramlintide is administered three times daily for a period of 14 days. See abstract; and page 493. The mean body weight ± SEM of diabetic patients included in Kolterman's (1996) method who were administered subcutaneously with 30 micrograms, 100 micrograms, and 300 micrograms of pramlintide, three times a day for 14 days, was 70.6 ± 2.7, 74.4 ± 2.5, and 75.7 ± 2.6 respectively. Therefore, the 70.6 to 75.7 kg insulin-taking diabetic patients from Kolterman's (1996) study qualify as human subjects in need of treatment for obesity as recited in the instant claims. Additionally, even BMI-wise, Kolterman's (1996) diabetic subjects meet the limitation 'a human subject .... in need of treatment for obesity' as recited in the instant claims, because the diabetic subjects included in Kolterman's method (1996) had a BMI of up to 27. See second full paragraph under 'Subjects, materials and methods'. Therefore, Kolterman's (1996) diabetic subjects having a BMI at least in the range of 24 up to 27 do qualify as diabetic subjects in need of treatment for obesity in light of what is known in the art. For example, Itasaka *et al.* teach that a BMI of 24.0 to 26.4 represents mild obesity and 26.4 and heavier (i.e., including a BMI of 26.4 to 27) represents obesity in humans (see abstract of Itasaka *et al.*). Kolterman's (1996) pramlintide composition did not comprise another obesity relief agent, but consisted of or consisted essentially of pramlintide. The pramlintide composition was injected subcutaneously to the human patients (see 'Study design') and therefore is expected to inherently contain a pharmaceutically acceptable carrier therein. The amount administered was 30 micrograms three times a day to 'about 0.1 milligrams' or 300 micrograms per day. See 'Study design'; Table 1; and paragraph there below. Kolterman's (1996) subcutaneous administration of the above-identified therapeutically effective amount of the amylin agonist, pramlintide or SEQ ID NO: 1, to diabetic human subjects taking insulin and weighing 70 kg or more, or having a BMI falling in the BMI range of 24 up to 27, necessarily serves as the Appellants' method of treating obesity by inhibiting weight gain or inducing weight loss in the human subject genus, as claimed currently, and therefore anticipates the instant

claims. Thus, the very active step recited in the instantly claimed method was disclosed and practiced by Kolterman *et al.* in April, 1996. Given that the method step in Kolterman's (1996) method and the instant claims are the *same*, and the amylin agonist analogue pramlintide administered and its amount administered are the *same*, Kolterman's (1996) method is expected to necessarily bring about the same weight gain-inhibiting (i.e., maintaining of existing body weight) or weight loss-inducing therapeutic effect in Kolterman's (1996) pramlintide-treated diabetic patients who are on insulin. Since the prior art clearly teaches the claimed method, any assertions of specific functional properties attributed to the amylin agonist pramlintide administered in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 1-7, 9, 11-14, 16 and 17 are anticipated by Kolterman *et al.* (1996). The publication of Itasaka *et al.* is **not** used as a secondary reference in combination with the reference of Kolterman *et al.* (1996), but rather is used to show that every element of the claimed subject matter is disclosed by Kolterman *et al.* (1996) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). Itasaka's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in 80 to 90% Kolterman's (1996) insulin-taking diabetic subjects administered with ^{25,28,29}Pro-human amylin, is necessarily present in the method thing described by Kolterman *et al.* (1996). The method of Kolterman *et al.* (1996) clearly anticipates the claimed method of the instant invention, because Kolterman *et al.* (1996) taught the very step of the instantly claimed method in diabetic human patients.

(E) Claims 7, 14 and 16 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Beumont *et al.* (US 5,321,008) ('008) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

It is noted that the limitation in the instant claim 16: 'a composition consisting essentially of an amylin or an amylin agonist', and the limitation in claim 14: 'method … comprising ….. wherein said

compound is not administered in conjunction with another obesity relief agent', do not exclude the administration of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent such as exendin etc. It is further noted that 'amylin agonist' is defined in the instant specification as a peptide or non-peptide compound that mimics the effect of amylin. See paragraph bridging pages 13 and 14 of the originally filed specification. Calcitonin and CGRP are described in the instant specification as sharing the food intake-suppressing action/effect of peripherally or centrally administered amylin. See paragraph bridging pages 9 and 10 of the originally filed specification.

Beumont *et al.* ('008) taught a method of subcutaneous administration to insulin-requiring humans who suffer from Type 1 or Type 2 diabetes mellitus a therapeutically effective amount of an amylin agonist *alone* such as calcitonin, or calcitonin and insulin, contained in a pharmaceutically acceptable carrier. See claims 11, 7, 13 and 4; lines 14-17 in column 5; lines 8-11 and 49-54 in column 12; and lines 34 and 35 in column 2. Claim 11 of the '008 patent is directed to the method of administering a therapeutically effective amount of the amylin agonist calcitonin to insulin-requiring humans with diabetes mellitus. The 'therapeutically effective amount' taught by Beumont *et al.* ('008) includes the typical dosage units of about 0.1 to 1 mg of calcitonin. See first full paragraph in column 13. The amount effective to treat obesity, the amount effective to inhibit weight gain, or the amount effective to induce weight loss encompassed in the instant claims as described in the instant application of about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls within the range of the therapeutically effective amount disclosed in the '008 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), 80 to 90% of diabetic patients used in the method disclosed in the '008 patent qualify as human patients in need of treatment for obesity. Therefore, the method of the '008 patent comprising the administration of about 0.1 to 1 mg of calcitonin to diabetic human species anticipates the instant claims. Given that the method step of the '008 patent and the instant claims is the same, and the amylin agonist administered and the amount administered are the same as the ones described in the instant specification, the method of the '008 patent is expected to bring about a obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect in Beumont's intrinsically obese, calcitonin-treated diabetic patients as defined in the instant invention. Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the teachings of the '008 patent, Beumont's ('008) method is expected to serve

necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain inhibiting effect, or weight loss-inducing effect. The Office's position that Beumont's ('008) method is the same as the Applicants' claimed method is based upon the fact that the method step, the amylin agonist calcitonin administered and its amount administered, the subcutaneous route by which the amylin agonist is administered, and the intrinsically obese diabetic human patient species to which the amylin agonist is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Beumont's ('008) method of administration of the above-identified therapeutically effective amount (i.e., dosage units of about 0.1 to 1 mg) of the amylin agonist calcitonin to 80 to 90% of intrinsically obese type 2 diabetic human subject species anticipates the instant claims. Given that the method step of the Beumont's ('008) method and the instant claims are the same, Beumont's ('008) method is expected to bring about the weight gain-inhibiting, weight loss-causing or obesity-treating effect in the intrinsically obese calcitonin-treated insulin-requiring human diabetic patients of the '008 patent. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist, calcitonin, in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 7, 14 and 16 are clearly anticipated by Beumont *et al.* ('008). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Beumont *et al.* ('008), but rather is used to show that every element of the claimed subject matter is disclosed by Beumont *et al.* ('008) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in 80 to 90% of Beumont's ('008) insulin-requiring diabetic subjects administered with calcitonin, is necessarily present in the method thing described by Beumont *et al.* ('008). The method of Beumont *et al.* ('008) clearly anticipates the claimed method of the instant invention, because Beumont *et al.* ('008) taught the very step of the instantly claimed method in the very same diabetic human patient species.

(F) Claims 7, 14, 16 and 17 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Gaeta *et al.* (US 5,686,411) ('411) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract).

The applied reference has a common assignee with the instant application. Based upon the

earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

The limitation 'consisting essentially of' in the instant claim 16 and the limitation 'method … comprising ….. wherein said compound is not administered in conjunction with another obesity relief agent' in claim 14 are interpreted as not excluding the presence of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent etc. in the recited composition.

Gaeta *et al.* ('411) taught a method of administering to mammals having diabetes mellitus, including patients seen by a medical practitioner, i.e., humans, a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (SEQ ID NO: 1 or pramlintide). See claims 34, 35 and 19; and lines 45-53 in column 7 of the '411 patent. Gaeta *et al.* ('411) taught the 'therapeutically effective amount' of the amylin agonist to include the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. See lines 53-59 in column 8. The amount effective to treat obesity, inhibit weight gain, or induce weight loss encompassed in the instant claims as described in the instant application, for example, about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls within the range of therapeutically effective amount of the amylin agonist disclosed in the '411 patent. Lines 9-14 of column 3 of the '411 patent describe that the limitation 'diabetes mellitus' includes *insulin-requiring* diabetes mellitus and that the administration is of amylin agonist analogue *alone*. The amylin agonist composition comprises a pharmaceutical carrier and the amylin agonist without insulin or glucagon. See lines 9-11 in column 7 and lines 37-39 in column 8. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), 80% to 90% of the diabetic patients administered with the amylin agonist ^{25,28,29}Pro-human amylin in the method disclosed by the '411 patent qualify as a human patient in need of treatment for obesity. Therefore, the method of the '411 patent comprising the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist ^{25,28,29}Pro-human amylin to diabetic humans anticipates the instant claims. Given that the method step of the '411 patent and the instant claims are the same, the amylin agonist, ^{25,28,29}Pro-human amylin, administered and the amount administered are the same, the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the teachings of the '411 patent. Gaeta's ('411)

method is expected to serve necessarily as the instantly claimed method and is expected to bring about a therapeutic effect, weight gain-inhibiting effect, and weight loss-inducing effect in the intrinsically obese ^{25,28,29}Pro-human amylin-treated insulin-requiring diabetic patients of Gaeta ('411). The Office's position that Gaeta's ('411) method is the same as the Appellants' claimed method is based upon the fact that the method step, the amylin agonist, ^{25,28,29}Pro-human amylin administered, the amount of the ^{25,28,29}Pro-human amylin administered, and the one intrinsically obese diabetic human patients to whom the ^{25,28,29}Pro-human amylin is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Gaeta's ('411) method of administration of the above-identified therapeutically effective amount (i.e., 0.1 to 5 mg, or 0.5 to 1.0 mg) of the amylin agonist ^{25,28,29}Pro-human amylin to intrinsically obese type 2 diabetic human subject species anticipates the instant claims. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist ^{25,28,29}Pro-human amylin used in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 7, 14 and 16 are clearly anticipated by Gaeta *et al.* ('411). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Gaeta *et al.* ('411), but rather is used to show that every element of the claimed subject matter is disclosed by Gaeta *et al.* ('411) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See *In re Samour* 197 USPQ 1 (CCPA 1978). Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., the prevalence of obesity in 80 to 90% of Gaeta's ('411) insulin-requiring diabetic subjects administered with ^{25,28,29}Pro-human amylin, is necessarily present in the method thing described by Gaeta *et al.* ('411). The method of Gaeta *et al.* ('411) clearly anticipates the claimed method of the instant invention, because Gaeta *et al.* ('411) taught the very step of the instantly claimed method in the very same diabetic human patient species.

Double Patenting Rejections

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759

F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970) and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R 3.73(b).

(G) Claims 7, 14, 16 and 17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta *et al*. ('411) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract).

The method of treatment claimed in claims 34 and 35 of the '411 patent includes administering to a mammal with diabetes mellitus a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (SEQ ID NO: 1 or pramlintide). The portion of the disclosure of the '411 patent at lines 45-53 in column 7 supporting the limitation 'mammal' does not exclude, but expressly includes a patient seen by a medical practitioner, i.e., humans. The portion of the disclosure of the '411 patent at second paragraph under 'Summary of the Invention' supporting the limitations 'diabetes mellitus' and 'administration of .... an amylin agonist analogue' include *insulin-requiring* diabetes mellitus and administration of an amylin agonist analogue alone (i.e., consisting of) or in conjunction with (comprising or consisting essentially of) insulin or a glucagon, i.e., not in conjunction with another obesity relief agent. The portion of the disclosure of the '411 patent at lines 53-59 in column 8 supporting the limitation 'therapeutically effective amount' of the amylin agonist includes the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. The amount effective to induce weight loss, i.e., treat obesity, encompassed in the instant claims as described in the instant application of about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, about 0.1 milligrams to about 1 milligram per day, or 300 micrograms per dose, falls within the range disclosed in the '411 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev, 80% to 90% of the human diabetic patients used in the method disclosed in the '411 patent qualifies as human

patients in need of treatment for obesity. Therefore, the method of the '411 patent comprising or consisting of the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist, ^{25,28,29}Pro-human amylin alone or in conjunction with insulin or glucagon, to diabetic human species anticipates the instant claims. Given that the method step of the '411 patent and the instant claims are the same, the amylin agonist analogue pramlintide used and its amount administered are the same, and the human diabetic patient used is the same, the method of the '411 patent is expected to bring about a weight gain-inhibiting effect, weight loss-inducing effect, or obesity-treating effect in the intrinsically obesity diabetic patient species administered with a therapeutically effective amount of the pramlintide as claimed in the instant invention. Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the disclosure of Gaeta *et al.* ('411), Gaeta's ('411) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the weight gain-inhibiting effect, weight loss-inducing effect, or obesity-treating effect.

(H) Claims 7, 14 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 13 of US patent 5,321,008 issued to Beumont *et al.* ('008) as evidenced by Tsanev (*Vutr. Boles* 23: 12-17, 1984, abstract).

The method of treatment claimed in claims 11 and 13 of the '008 patent includes administering to a human with type 2 diabetes mellitus a therapeutically effective amount of the amylin agonist, calcitonin. The portion of the disclosure of the '008 patent at lines 14-17 in column 5; lines 8-11 and 49-54 in column 12; and lines 34 and 35 in column 2 that supports the claims includes subcutaneous administration to an insulin-requiring human who suffers from Type 1 or Type 2 diabetes mellitus a therapeutically effective amount of an amylin agonist *alone* such as calcitonin (i.e., consisting of), or calcitonin and insulin (i.e., comprising or consisting essentially of), contained in a pharmaceutically acceptable carrier. The portion of the disclosure of the '008 patent at first full paragraph in column 13 of the '008 patent supporting the 'therapeutically effective amount' includes the typical dosage units of about 0.1 to 1 mg of calcitonin. The amount effective to treat obesity, or the amount effective to induce weight loss encompassed in the instant claims as described in the instant application, for example, about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls within the range of the therapeutically effective amount disclosed in the '008 patent. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as

disclosed by Tsanev (see abstract), 80 to 90% of *insulin-requiring* human diabetic patients used in the method in the above-identified of the '008 patent qualify as human patients in need of treatment for obesity. Therefore, the method of the '008 patent comprising the administration of about 0.1 to 1 mg of calcitonin to insulin-requiring diabetic human species anticipates the instant claims. Given that the method step of the '008 patent and the instant claims is the same, and the amylin agonist calcitonin administered and the amount administered are the same, and the human diabetic patient species to whom calcitonin is administered is the same as the one described in the instant application, the method claimed in the '008 patent is expected to bring about an obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect in the intrinsically obese calcitonin-treated diabetic patient species of the '008 patent. Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the teachings of the '008 patent, Beumont's ('008) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Beumont's ('008) method of administration of the above-identified therapeutically effective amount (i.e., dosage units of about 0.1 to 1 mg) of the amylin agonist of calcitonin to 80 to 90% of intrinsically obese type 2 diabetic human subject species anticipates the instant claims.

(10) Response to Appellants' Arguments

(I) In response to the rejection of claims 1-7 and 9-17 made in paragraph 29 of the Office Action mailed 02/11/08 and maintained in paragraph 14 of the Office Action mailed 04/30/08 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the full scope, Appellants submit the following arguments.

(a) The proper standard for determining compliance with the enablement requirement is whether the specification provides sufficient information to permit one skilled in the art to make and use the claimed invention. *United States v. Telectronics, Inc.,* 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). The test of enablement is not whether experimentation is necessary, but rather whether any experimentation that is necessary is undue. A considerable amount of experimentation is permitted, provided that it is merely routine, or provided that the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands,* 8 USPQ2d 1400, 1404 (Fed. Cir.

1988). A specification that discloses how to make and use a claimed invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented "must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana, 51* F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995) (quoting *In re Marzocchi,* 439 F.2d 220, 223,169 U.S.P.Q. 367, 369 (C.C.P.A. 1971).

(b) Regarding the quantity of experimentation needed, the standard for determining enablement is whether the experimentation needed to practice the invention is undue or unreasonable. *Mineral Separation v. Hyde,* 242 U.S. 261,270 (1916). One of ordinary in them would have the ability to select amylin and amylin agonist peptides for use in the claimed methods without undue experimentation in view of the specification. Methods of synthesis of a defined group of compositions useful in the claimed methods are provided or known in the art, as are methods of administration and methods of weight determination.

(c) Regarding the amount of direction or guidance presented, the specification *broadly* discloses that the claimed amylin or amylin agonist compounds are useful in the treatment of obesity in a subject in need thereof. There is express guidance as to modes of administration, therapeutic dosages, mechanisms for assessing therapeutic efficacy, as well as a working example to demonstrate the statistically significant ability of an exemplary amylin compound to treat obesity in a human subject in need thereof. In the working example, the human subjects were Type 2 diabetics. The working example illustrated Type 2 diabetic subjects taking insulin does not render the scope of enablement limited to this subject population. Rather, it demonstrates that in a particularly difficult to treat, obese subject population (Type 2 diabetic subjects taking insulin), an exemplary amylin compound is therapeutically effective in the treatment of obesity. Taken together with the teachings of the specification (e.g., page 18, paragraph 3 to page 23, paragraph 2), the working example provides a base-line approach for establishing therapeutic efficacy of exemplary amylin compounds within the context of the presently claimed methods. Utilizing similar study structures, Appellants have in fact established that exemplary amylin compounds are effective in the treatment of obesity in non-diabetic subjects as well (see, e.g., IDS entries AZ1, AZ2, AZ4 and AZ5 of Aronne, et *al. and* Smith, et *al.* of record). This evidence confirms the teachings of the specification, and demonstrates that Appellants' working example in fact

provides enablement of the efficacy of a particularly difficult to treat, chronically obese subject population.

(d) The Office is impermissibly attempting to limit the scope of enablement to the scope of the working examples. Based on the extensive guidance provided in the specification, including the human clinical study results, as well as the high level of skill in the art, the skilled artisan would be able to evaluate efficacy of amylin compounds in accordance with the methods of the inventions to ascertain therapeutically effective amounts of the recited amylin compounds. The Office's characterization of Example 1 only serves to underscore the enablement of the claims in this regard. Example 1 describes a clinical study wherein routine dosages were evaluated in human clinical subjects to ascertain a therapeutically effective dose as well as effective administration regimens. The working examples, in combination with the disclosure of the specification and knowledge of one skilled in the art, amply enable the full scope of the invention as presently claimed.

(e) With respect to reasons for doubting the objective truth of the specification based on Rink's disclosure as relied upon by Appellants' prior admission in their Appeal Brief filed July 2000, when read in context, it is clear that Rink only contemplates amylin-induced appetite suppression in rodents, not in humans. Rink does not describe the treatment of obesity in humans using amylin or an amylin agonist as required by the claims of the present invention.

(f) Regarding the nature of the invention, Appellants agree with the Office's assertion that the nature of the invention is pertinent to the treatment of obesity in a human subject in need of such treatment comprising or consisting of administering an amylin, an amylin agonist, or an amylin agonist analogue composition or compound in an amount effective to inhibit weight gain or induce weight loss in the subject. Specifically, the invention contemplates the treatment of obesity in human subject in need of treatment by the administration of an amylin or amylin agonist. Indeed, Appellants discovered that amylin or agonists thereof can be used for the treatment of obesity.

(g) The relative skill of one or ordinary skill in the art to which the invention pertains is very high. Regarding the state of the prior art, Appellants agree in part with the Office's characterization of obesity or adiposity as a 'chronic disease' that is highly prevalent in modern society which is strongly associated with multiple conditions including diabetes mellitus, insulin resistance, hypertension, etc. However, the Office appears to have failed to note that *the prior art does not disclose the subject*

matter of the claims of the present application taken as a whole. Indeed, it was Appellants' discovery that amylin or amylin agonists could be administered to a human subject in need of treatment for obesity. In this respect, one of ordinary skill in the art would have the ability to select amylin and amylin agonist peptides for use in the claimed methods without undue experimentation. Indeed, amylin compounds recited in the claims are generally recognized as a defined class of compounds, and the specification provides ample direction and guidance to those skilled in the art with regard to the identification of such amylin compounds useful in the context of the claimed methods.

(h) Regarding the predictability or unpredictability of the art, the Office alleges that the state of the art with regard to the use of amylin in obesity is unpredictable and that Baron *et al.* and Ratner *et al.* indicate the impracticability of using amylin as a therapeutic agent. Both Baron *et al.* and Ratner *et al.* actually support enablement of the claimed invention. Whether native human amylin is suitable for use as a commercial drug product is not a proper standard for judging the enablement of the present claims. Given the teachings of the instant specification, one of ordinary in the art would have the ability to select amylin and amylin agonist peptides for use in the claimed methods without undue experimentation. This further confirms that both amylin and amylin agonists are well known compounds that have been widely characterized. Given this, one of ordinary skill in the art would have the requisite skill to practice the invention commensurate in scope with the claims without undue experimentation.

(i) Regarding the breadth of the claims, in rejecting the claims the Office has impermissibly attempted to limit the invention to the scope of the examples. Such a standard is legally incorrect. As set forth in MPEP 3 2164.02, "[f]or a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation." Tables I - II and Examples 1-8 disclose data relating to the claimed methods and exemplary amylin compounds. Alone, this disclosure is sufficient such that one of ordinary skill in the art at the time the invention was made would have the ability to practice the invention commensurate in scope with the claims. Appellants disagree with the Office's assertion that the only amylin agonist analogue species within the recited broad genus that is being used for inducing weight loss in humans is pramlintide. Again, the Office appears to be focusing on Example 1 rather than the teachings of the specification as a whole and the level of ordinary skill in the art. In

this regard, it is noted that amylin compounds recited in the claims are generally recognized as a defined class of compounds, and the specification provides ample direction and guidance to those skilled in the art with regard to the identification of such amylin compounds useful in the context of the claimed methods. Furthermore, the specification is replete with examples of amylin agonists, including functional variants, fragments, and derivatives of amylin and amylin agonists. See e.g. specification page 13 paragraph 4 to page 17, paragraph 1. Given at least the discussion in the background concerning amylin agonists, as well as the description of SEQ ID NO: 12-17, one of ordinary skill in the art having read the specification would have the ability to select known amylin agonists without undue experimentation. Moreover, to the extent that any additional experimentation may be required, the performance of routine and well known steps cannot create undue experimentation even if it is laborious. See *In re Wands* (Id.); *In re Angstadt,* 190 USPQ 214 (CCPA 1976). Given the knowledge in the art, and based on the guidance provided in the specification regarding the extensive exemplary embodiments of amylin compounds, receptor binding assays and other assays for determining amylin activity, including the soleus muscle assay, and exemplary clinical study designs, additional therapeutically active amylin agonists can be identified within the context of the present claims without the need for undue experimentation. The specification provides numerous examples of compounds within the scope of the recited genus, and guidance with regard to assays and clinical studies in the examples useful to evaluate the efficacy of the compounds in the methods of the present invention. Based on such guidance, one of skill in the art would be able to practice the claimed invention with only routine experimentation.

(j) Claim 2 requires that the amylin agonist of claim 1 is an amylin agonist analogue. As generally understood by those of skill in the art, amylin analogues are compounds that are structurally related to the reference compound, i.e., amylin. As explained in the specification and understood by those having ordinary skill in the art, *an amylin analogue can have one or more amino acid substitutions, deletions, inversions, or additions compared to a native or naturally occurring amylin.* Furthermore, claim 2 merely requires that the amylin analogue is an amylin agonist analogue. In accordance with the claims and the knowledge of those of ordinary skill in the art, the recited amylin agonist analogues are both structurally and functionally defined. Hence, claim 2 is enabled. With regard to the Office's position on the scope of various claim terms and transitional phrases, various claim terms such as obesity and administering are discussed in a broad context. While Appellants do

not necessarily agree with the exact definition provided by the Office, Appellants do acknowledge the broad scope of such terms commensurate with the present specification. With regard to the use of traditional transitional phrases such as 'comprising', 'consisting of' and 'consisting essentially of', such language has been used in the traditional context. Within the context of the claimed methods for treating obesity, such terms of art would have their traditional meanings and limitations with regard to claim elements relevant to the treatment of obesity. However, such traditional claim terms would have no bearing on components, steps, or elements outside of the claimed scope of the treatment of obesity.

The Office submits the following response to Appellants' arguments:

In the instant application, except for one amylin agonist species, pramlintide, Appellants have not established that a representative number of the vast number of exemplary amylin compounds encompassed within the scope of the claims is indeed effective in the treatment of obesity in diabetic or non-diabetic subjects. With regard to the use of amylin and non-pramlintide amylin agonists in treatment of obesity in humans, the Office agrees with Appellants that *the prior art does not disclose the subject matter of the claims of the present application.* It is because of this reason, one of skill in the art would look into Appellants' specification for specific guidance and direction to practice the full breadth of the instantly claimed method, but is lacking. A mere description of methods of synthesizing amylin agonist peptides is not sufficient to enable the full scope of the method of treating obesity as claimed. Even if a skilled artisan selected some of the exemplary amylin agonist analogues recited in the instant specification, there is no predictability that said non-pramlintide amylin agonist analogues would have the therapeutic effect against a particularly difficult to treat obese diabetic or morbidly obese human subjects and is usable in the claimed method.

With regard to Appellants' statement that an amylin analogue can have one or more amino acid substitutions, deletions, inversions, or additions compared to a native or naturally occurring amylin, it should be noted that, other than pramlintide, no amylin analogues having one or more amino acid substitutions, deletions, inversions, or additions compared to a native or naturally occurring amylin have been shown to be effective in treating obesity and therefore usable in the methods as claimed. How to make one or more the one substitutions, deletions, inversions, or additions in an amylin analogue in such a way that the resultant products would still have weight loss-inducing or weight gain-inhibiting, or obesity-inducing effect is neither taught by Appellants, nor is it known in the state of the art.

With regard to the quantity of experimentation needed, the standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: 'is the experimentation needed to practice the invention undue or unreasonable'. That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In the instant case, no guidance or direction has been provided in the instant specification so that one could predict which of the amylin agonist analogue species other than pramlintide would have the requisite therapeutic effect against obesity. Because there is no way to predict *a priori* which amylin, amylin agonists, or amylin agonist analogues from the specification or from the chemical structures alone would be therapeutically active against obesity in diabetic or non-diabetic humans subjects, including morbidly obese human subjects, an extraordinary amount of trial and error experimentation is required to identify the obesity-treating amylin agonist analogue species. Assuming *arguendo* that the experimentation required is routine, and if one of skill in the art screens innumerable non-pramlintide amylin agonist species or amylin agonist analogue species currently encompassed within the recited genus, including those disclosed in Examples 2 and 3 or Table II of the instant invention, using receptor binding assays and assays for amylin activity, there is absolutely no predictability that a non-pramlintide amylin agonist having amylin activity would have a wait gain-inhibiting effect, weight loss-inducing effect, obesity-relieving effect, or food intake-reducing effect given the Applicants' admission that amylin itself has no effect on food intake. Given this and the lack of showing within the instant specification as explained above, the weight loss-inducing or weight gain-inhibiting effect of any amylin or any non-pramlintide amylin agonist analogue mimicking effect(s) of amylin, administered alone or as an adjunct to insulin therapy, to an obese diabetic or obese non-diabetic human subject, is simply not predictable. Applicants have provided no guidance with regard to the use of extraordinarily large genus of amylins, amylin agonists, and amylin agonist analogues in the treatment of obesity in humans. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states: 'The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art'. The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or *use* the invention. The more is known in the prior art about the nature of the invention, how to make, *and* how to use the invention, and the more predictable the art is, the less

information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling' (MPEP 2164.03). MPEP also states that physiological activity can be considered inherently unpredictable. Whether the specification would have been enabling *as of the filing date* involves consideration of the nature of the invention, the state of the prior art, and the level of skill in the art. The initial inquiry is into the nature of the invention, i.e., the subject matter to which the claimed invention pertains. The nature of the invention becomes the backdrop to determine the state of the art and the level of skill possessed by one skilled in the art. The state of the prior art is what one skilled in the art would have known, *at the time the application was filed*, about the subject matter to which the claimed invention pertains. The relative skill of those in the art refers to the skill of those in the art in relation to the subject matter to which the claimed invention pertains *at the time the application was filed*. See MPEP § 2164.05(b). None of the post-filing references and abstracts cited by Appellants represents the state of the art *at the time of filing*. The abstracts of Aronne *et al*. (*Obesity* 14: A17, 2006) and Smith *et al*. (*Diabetes* 56: A88, 2007) submitted by Appellants are silent about the diabetic or non-diabetic status of the subjects included in the study. Both are limited to the use of the single amylin agonist analogue species, pramlintide in the method described therein. The post-filing teachings of Aronne *et al*. (*J. Endocrinol. Metabol*. 92: 2977-2983, 2007) and Smith *et al*. (*J. Am. J. Physiol. Endocrinol. Metabol*. 293: 620-627, 2007) submitted by Appellants are also limited to the use of one amylin agonist analogue species, pramlintide, for reducing caloric intake and meal size, or for reducing body weight. These two post-filing publications support the Office's position on the lack of enablement of the full scope of the instant claims by confirming that even about a decade after the effective filing date of the instant application, the only amylin agonist analogue species within the recited broad genus that is being used for inducing weight loss in humans is pramlintide.

With regard to Appellants' arguments on the reasons for doubting the objective truth of the specification and Appellants' comments on the limitation 'an amount effective to treat obesity' particularly in connection with amylin, a nonpramlintide amylin agonist, a non-pramlintide amylin agonist analogue, a salt of amylin, and a salt of amylin agonist, the following should be noted. The post-filing references of Aronne et *al.* and Smith et *al.* cited by Appellants do not show that administration of any amylin or any non-pramlintide amylin agonist analogue as claimed in the instant

claims results in inhibition of weight gain or induction of weight loss in diabetic or non-diabetic human subjects in need of treatment of obesity. As set forth above, at the time of the invention, amylin at a dose varying from about 0.1 to 10 mg was administered to treat patients suffering from anorexia or patients deficient in adipose tissue. See claims and page 13 of Rink *et al.* (WO 9220367). Note that the instantly recited 30 to 300 micrograms per dose of amylin falls within Rink's anorexia-treating dose. The scope of Rink's disclosure includes mammals and therefore does not exclude humans. Appellants themselves have established the direct relevance of Rink's ('106) disclosure to humans via their following statements. Appellants have previously gone on the record with the following (see pages 9, 13 and 14 of Appellants' Appeal Brief filed July 2000) [Emphasis in original]:

> .... THE RINK PATENT PROVIDES THAT AMYLIN AND AMYLIN AGONISTS ADMINISTERED AS DESCRIBED AND CLAIMED IN THE PRESENT APPLICATION HAVE "NO MEASURABLE EFFECT" ON FOOD INTAKE.
>
> .... the Rink patent reports that a 1.0 μg/kg dose (**equivalent to about 70μg/dose in an adult human**) had no effect on food intake. [Emphasis in bold added]

Therefore, there was no predictability that administration of a dose varying from about 0.1 to 10 mg of amylin to a human patient would have resulted in inhibition of weight gain or induction of weight loss. Instead of weight loss, one of skill in the art would have expected induction of weight gain. This is yet another reason for doubting the objective truth of the specification. Furthermore, with the art-reported instability of amylin in solution and its tendency to aggregate, one of skill in the art would not have been able to determine an amount effective to reduce weight loss, inhibit weight gain, or relieve obesity without undue experimentation. In view of this, Appellants' description of exemplary amylin agonist compounds alone is insufficient to enable the full scope of the claimed invention. Because of the admitted therapeutic efficacy of amylin against anorexia, one of skill in the art could not have predictably selected non-pramlintide amylin agonist species or non-pramlintide amylin agonist analogue species for treating obesity without considerable amount of undue experimentation. Thus, in view of level of skill, the state of the art at the time of the invention, and the information in the specification, one of skill would *not* expect that the recited genus could be used in that manner without undue experimentation.

In sum, contrary to Appellants' allegation, a *prima facie* case of lack of scope of enablement has been established by providing sufficient references and specific technical reasons along with the

documentation of Appellants' own previous statements. Given the knowledge in the art of the therapeutic effect of amylin against anorexia despite its amylin agonistic characteristics as measured by receptor binding assays and the soleus muscle assay etc., the breadth of the claims, the lack of predictability when viewed in combination with Rink's ('367) showing that the administration of about 0.1 to 10 mg amylin is therapeutic against anorexia, Appellants' own previous acknowledgment that administration of amylin would have lead to *weight gain* rather than *weight decrease* as was known at the time of the invention, Appellants' own previous acknowledgment that amylin and amylin agonists have no measurable effect on food intake, the lack of working examples enabling the full scope of the claimed invention, a considerable amount of non-routine undue experimentation would have been required to reproducibly practice the full scope of the invention, as claimed. Instant claims do not meet the scope of enablement provisions of 35 U.S.C. § 112, first paragraph.

For the reasons delineated above, the art rejection should be sustained.

(II) In response to the rejection of claims 1, 7, 14 and 16 made in paragraph 28 of the Office Action mailed 02/11/08 and maintained in paragraph 13 of the Office Action mailed 04/30/08 under 35 U.S.C § 112, first paragraph, as containing new matter, Appellants submit the following arguments. The Office's rebuttal is provided therein below.

(a) With regard to the Office's lack of descriptive support for the transitional term of art 'consisting' in claim 1, Appellants argue that the term 'consisting' used in claim 1 is a term of art that need not be specifically recited in the specification.

However, it should be noted that it is not merely the limitation 'consisting' in claim 1 that is pertinent to the instant rejection. The new matter rejection pertains to something more than the use of the term 'consisting' in claim 1. Claim 1, as amended, includes the phrase: 'method of treating obesity in a human subject *consisting of administering* to said subject *an amount effective to inhibit weight gain* or induce weight loss in said human subject of a *composition comprising* an amylin or an amylin agonist … and a pharmaceutically acceptable carrier' [Emphasis added]. Claim 1 includes the limitation: 'method of treating obesity …. consisting of administering …. an amount effective to inhibit weight gain or induce weight loss …… of composition comprising an amylin or an amylin agonist and a pharmaceutically acceptable carrier'. A method of treatment of obesity 'consisting of' such an administration step *excludes,* for example, simultaneous insulin administration, or insulin

administration minutes or hours before or after the administration. However, neither the original six claims, nor the description of the methods of treatment of the instant invention support such a method of treating obesity 'consisting of' administering an effective ..... composition comprising an amylin or an amylin agonist and a pharmaceutically acceptable carrier. For example, the originally filed specification at lines 6-8 of page 9 of the specification states [Emphasis added]:

> The present invention is directed to novel methods for treating or preventing obesity in humans *comprising* the administration of an amylin or an amylin agonist, the amylin agonist analogue ^{25,28,29}Pro-human amylin.

Pages 30-31 and Table I describe a statistically significant reduction in the mean baseline weight seen after the subcutaneous administration of 60 micrograms TID or 60 micrograms QID of one specific amylin agonist analogue species, pramlintide, to type II diabetic subjects for four weeks, wherein said pramlintide administration was accompanied *with the continued administration of insulin*. The method of treatment of obesity as described in the originally filed specification comprised insulin treatment *and* the administration of a specific dose of pramlintide to type II diabetic patients. This however does not provide descriptive support for the now claimed method of treating obesity in a human in need of treatment for obesity, said method 'consisting' of administering to said subject an amount of a composition as recited comprising an amylin or any amylin agonist and a pharmaceutically acceptable carrier, wherein said amount of the composition is effective to inhibit weight gain or induce weight loss in said subject. It is noted that Appellants have advanced no substantive arguments other than stating that the term 'consisting' in claim 1 is a term of the art that need not be specifically recited in the specification.

(b) Appellants contend that the support for the 'concept' of inhibiting weight gain or inducing weight loss may be found in the specification at lines 9-16 on page 9 of the specification, which discloses the following (Emphasis added by Appellants):

> In one aspect, the invention is directed to a method of treating obesity in a human subject comprising administering to said subject an effective amount of an amylin or such an amylin agonist. By "treating or preventing" is meant the management and care of a patient for the purpose of combating the disease, condition or disorder, and includes the administration of an amylin or an amylin agonist to prevent the onset of symptoms or complications, alleviating the symptoms or complications, or eliminating the disease condition or disorder. Treating or preventing obesity therefor includes the inhibition of weight gain and inducing weight loss in patients in need thereof.

Appellants state that further support for the amount of amylin or amylin agonist contemplated in the claims may be found, e.g., at specification page 22, last two lines: "[t]herapeutically effective amounts of an amylin or amylin agonist, such as an amylin agonist analogue, for use in the control of

obesity are those that decrease body weight." The amount effective to treat obesity of a composition comprising the required amylin or amylin agonist of the invention is determined by routine methods of pharmaceutical research, and that effectiveness is due to the amylin or amylin agonist in the composition administered to the human subject in need of treatment for obesity.

However, these parts of the specification do not and cannot provide descriptive support for: (a) the claimed 'method of treating obesity in a human subject *consisting of administering* to said subject *an amount effective to inhibit weight gain* or induce weight loss in said human subject of a *composition comprising* an amylin or an amylin agonist …' in claim 1; (b) for the limitations 'an *amount effective to inhibit weight gain … of a composition comprising* an obesity relief agent ….' in claim 7; and (c) the limitations '*salts thereof* …. administered in an amount effective to treat obesity …. by *inhibiting weight gain*' in claim 14 [Emphasis added]. A therapeutically effective amount of an amylin or amylin agonist such as amylin agonist analogue that decreases body weight is not the same in scope as 'an amount of *a composition comprising* an amylin or an amylin agonist effective to *inhibit weight gain* or *induce weight loss*', because the composition recited in claim 1 is allowed to 'comprise' therein other anti-obesity agents other than an amylin or amylin agonist such as exendin, a lipase inhibitor, peptide YY etc. The language 'composition comprising' represents open-ended claim language and therefore, does not exclude additional, unrecited elements. See MPEP 2111.03 [R-1]. See *Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986)*; *In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ('comprising' leaves 'the claim open for the inclusion of unspecified ingredients *even in major amounts'*) [Emphasis added]. Therefore, the limitation 'composition comprising' in claim 1 allows the inclusion of additional anti-obesity agents to be present in the recited composition. Therefore, an amount of a composition 'comprising' amylin or amylin agonist would include an amount of other anti-obesity agents such as exendin, CCK, peptide YY, or other elements such as insulin, glucgon etc. comprised within the composition. Contrary to Appellants' assertion, the effectiveness of the recited composition cannot be due to amylin or amylin agonist *alone* comprised in the composition.

(c) With regard to the lack of support in claim 14 for 'salts' of amylin or amylin agonist administered in an amount effective to treat obesity by inhibiting weight gain or inducing weight loss in a human subject in need of treatment of obesity, wherein the salt compound is not administered in

conjunction with another obesity relief agent, Appellants assert that support for the 'concept of salts' of the compounds of the invention in a *broad sense* may be found at lines 20 and 21 of the specification. Lines 20-21 from page 21 of the instant specification are reproduced below:

> the compounds referenced above may form salts with various inorganic and organic acids and bases. Such salts include salts prepared with organic and inorganic acids, for example,

However, what is claimed in claim 14 is not a salt of amylin or amylin agonist, but a method of administering a salt compound of an amylin or amylin agonist in an amount effective to treat obesity by inhibiting weight gain or inducing weight loss in a human subject in need of treatment of obesity, wherein the salt compound is not administered in conjunction with another obesity relief agent. There is lack of support for such a method.

(d) Appellants acknowledge that the dependent claims 2-6, 9-13, 15 and 17 depend from the independent claims 1, 7, 14 and 16, but argue that the Office has provided no express rejection of these dependent claims and therefore the rejection is moot.

As acknowledged by Appellants, claims 2-6, 9-13, 15 and 17 are dependent claims depending from the rejected claims 1, 7, 14 and 16. Since dependent claims are construed to contain *all the limitations* of the claim upon which they depend, it is appropriate to include the dependent claims in the rejection statement.

For the reasons delineated above, the art rejection should be sustained.

(III) In response to the rejection of claims 1-7, 9-14, 16 and 17 made in paragraph 33 of the Office Action mailed 02/11/08 and maintained in paragraph 15 of the Office Action mailed 04/30/08 under 35 U.S.C § 102(a) as being anticipated by Kolterman *et al.* ('220) as evidenced by Tsanev, Appellants submit the following arguments.

(a) Appellants cite case law and MPEP §2131 and assert that in order to anticipate a claim, a single prior art reference must provide each and every element set forth in the claim, and that the identical invention must be shown in complete detail as it is contained in the claim.

(b) Kolterman '220 merely describes the use of an amylin agonist (i.e., pramlintide) for treating type II diabetes mellitus. Kolterman '220 merely demonstrates that administration of an amylin agonist significantly reduces postprandial plasma glucose concentrations in patients with type II diabetes mellitus. Kolterman '220 does not teach the use of an amylin or an amylin agonist for treating

obesity or demonstrate a reduction in body weight in those patients administered an amylin or an amylin agonist. Kolterman '220 is silent with regard to the effect of an amylin or an amylin agonist on body weight.

(c) Kolterman '220 at page 7, first paragraph, discloses that the hyperglycemia associated with Type II diabetes can sometimes be reserved or ameliorated by diet or weight loss. With respect to the use of amylin or amylin agonists for treatment of obesity in a subject in need thereof, Kolterman '220 is silent. Whether or not Kolterman '220 discloses that weight loss is beneficial is irrelevant, at least because the Office has failed to state a nexus between administration of an amylin or agonist thereof and treatment for obesity.

(d) In an attempt to cure the deficiency in Kolterman '220, the Office relies on Tsanev to allegedly provide evidence that 80-90% of diabetic patients are obese. However, the 80-90% of obese diabetic patients alleged by Tsanev falls short of the 100% (i.e., always, under any circumstances) criterion required by the claims and required by the law. Thus, Kolterman '220 as evidenced by Tsanev does not provide each and every element of the claimed invention, at least because Kolterman '220 (with or without Tsanev) is silent with respect to treatment of obesity with amylin or agonists thereof, or the intended population for treatment (i.e., human subject in need of treatment for obesity) of the current claims.

Appellants' arguments have been carefully considered, but are not persuasive. Clearly, the Office has set forth a *prima facie* case of anticipation.

Contrary to Appellants' assertion, the prior art method necessarily includes *all* of the elements of the instant claims. As set forth previously, Kolterman *et al.* ('220) taught a method of administering to an insulin-taking type II diabetic human subject a dose of 10, 30, 50, 60 or 150 micrograms per day (i.e., the amount falling in the range recited in the instant claims) of the amylin agonist composition, pramlintide or $^{25, 28, 29}$pro-h-amylin, also known as AC137 (i.e., SEQ ID NO: 1), i.e., the same amylin agonist administered in the instantly claimed method. The composition consists of pramlintide and a pharmaceutically acceptable carrier, and is administered in single or multiple doses, for example, of about 30 micrograms QID, or about 60 micrograms TID or QID, i.e., an amount effective to inhibit weight gain or induce weight loss. See pages 9-11; paragraph bridging pages 20 and 21; page 21; first paragraph on page 19; lines 8-10 on page 19; and the first row reciting 'Insulin-Treated Patients' in each Table of Kolterman *et al.* ('220). Pramlintide is administered subcutaneously 1-4 times a day,

before meals. See pages 9 and 22. Kolterman *et al.* ('220) additionally taught that the presence of obesity is a characteristic of 'most patients with Type II diabetes mellitus' (i.e., in need of treatment of obesity). See page 10. Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the teachings of Kolterman *et al.* ('220), Kolterman's ('220) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain inhibiting effect, or weight loss-inducing effect.

The Office's position that Kolterman's ('220) method is the same as the Appellants' claimed method is based upon the fact that the method step, the pramlintide compound administered, the amount of the compound administered, the route by which the compound is administered, and the intrinsically obese type II diabetic human patient species to which the pramlintide compound is administered, are the *same* in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Kolterman's ('220) method of administration of the above-identified therapeutically effective amount (i.e., about 30 micrograms QID, or about 60 micrograms TID or QID, or a dose of 10, 30, 50, 60 or 150 micrograms per day) of the amylin agonist ^{25,28,29}Pro-human amylin to intrinsically obese type 2 diabetic human subject species anticipates the instant claims. That 10-20% of Kolterman's ('220) diabetic patients, also to whom pramlintide is administered, are not expected to be obese is not relevant since an anticipatory reference does not have teach every species or every embodiment encompassed by the scope of the claims. Given that the method step of the Kolterman's ('220) method and the instant claims are the same, Kolterman's ('220) method is expected to bring about weight gain-inhibiting or weight loss-causing therapeutic effect in the intrinsically obese pramlintide-treated type II diabetic patient. Contrary to Appellants' assertion, the prior art method necessarily includes *all* of the elements of the instant claims. That the determination of inherency in the instant case is certainly not established by probabilities or possibilities is further evidenced by the teachings of Thompson *et al.* (May 1997). Thompson *et al.* (May, 1997) showed that a method of subcutaneous administration of pramlintide, i.e., $^{25, 28, 29}$pro-h-amylin, an analog of human amylin, i.e., an amylin agonist, to patients with type II diabetes requiring insulin, at a dose 60 micrograms QID (i.e., four times a day) or TID (i.e., three times a day) not only improved glycemic control in these patients, but ***also decreased body weight*** concurrently (see abstract). Therefore, Kolterman's ('220) method necessarily served as a method of treating obesity. Since the prior art clearly teaches the instantly claimed method, any assertions of

specific functional properties attributed to the amylin agonist pramlintide administered in the claimed method are merely inherent and do not necessarily make the claimed method patentable. *Ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993) (The Board rejected a claim directed to a method for protecting a plant from plant pathogenic nematodes by inoculating the plant with a nematode inhibiting strain of *P. cepacia*. A U.S. patent to Dart disclosed inoculation using *P. cepacia* type Wisconsin 526 bacteria for protecting the plant from fungal disease. Dart was silent as to nematode inhibition but the Board concluded that nematode inhibition was an inherent property of the bacteria. The Board noted that applicant had stated in the specification that Wisconsin 526 possesses an 18% nematode inhibition rating.). In the instant application, the obesity-relief or weight loss-induction is an inherent property inseparable from the administered pramlintide. The two structurally identical pramlintide compounds administered in the two methods (i.e., the prior art method and the instant method) cannot have mutually exclusive properties. The same two methods cannot have mutually exclusive results.

To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. The alleged failure of Kolterman ('220) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Kolterman's ('220). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

It is a commonly known fact in the art that type II diabetic patients (80-90% of whom are known to be obese) are 'in need of' obesity. Appellants themselves characterize Type 2 diabetic

subjects taking insulin as a particularly difficult to treat obese subject population. See top of page 14 of Appellants' after-final amendment. With regard to the Appellants' statement that Tsanev's disclosure that 80-90% of diabetic patients are obese falls short of the 100% (i.e., always, under any circumstances), the following must be noted. 'A generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus'. The species in that case will anticipate the genus. *In re Slayter*, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989). A genus does not always anticipate a claim to a species within the genus. However, when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. In *In re Sivaramakrishnan*, 673 F.2d 1383, 213 USPQ 441 (CCPA 1982), the claims were directed to polycarbonate containing cadmium laurate as an additive. The court upheld the Board's finding that a reference specifically naming cadmium laurate as an additive amongst a list of many suitable salts in polycarbonate resin anticipated the claims. The applicant had argued that cadmium laurate was only disclosed as representative of the salts and was expected to have the same properties as the other salts listed while, as shown in the application, *cadmium laurate had unexpected properties*. The court held that it *did not matter that the salt was not disclosed as being preferred, the reference still anticipated the claims* and because the claim was anticipated, *the unexpected properties were immaterial*. Although the instant claims are method claims, in the instant application, the prior art disclosure of a method comprising or consisting of the administration of 30 or micrograms of the amylin agonist, ^{25,28,29}Pro-human amylin, to 80-90% of the human diabetic patients anticipates the instantly claimed method. The claims are anticipated because the administered ^{25,28,29}Pro-human amylin also inherently exerted obesity-relieving properties in said method. See also *Ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993) (The Board rejected a claim directed to a method for protecting a plant from plant pathogenic nematodes by inoculating the plant with a nematode inhibiting strain of *P. cepacia*. A U.S. patent to Dart disclosed inoculation using *P. cepacia* type Wisconsin 526 bacteria for protecting the plant from fungal disease. Dart was silent as to nematode inhibition but the Board concluded that nematode inhibition was an inherent property of the bacteria. The Board noted that applicant had stated in the specification that Wisconsin 526 possesses an 18% nematode inhibition rating.). In the instant application, the obesity-relief or weight loss-induction is an intrinsic property inseparable from the administered pramlintide. The two structurally identical pramlintide compounds administered in the two methods (i.e., the prior

art method and the instant method) cannot have mutually exclusive properties. As set forth above, this is evidenced by the teachings of Thompson *et al.* (May 1997).

In the instant application, it is important to note that the *human patients used in the instant specification for treatment of obesity via administration of pramlintide are indeed type II diabetic human patients*. Thus, the prior art disclosure is commensurate in scope with the instant disclosure with regard to the type 2 diabetic human subject population used, the pramlintide compound administered, the amount and the frequency of pramlintide administered, to the type 2 diabetic human patients.

In the instant case, the claims are drawn to a method of treatment of obesity that uses generic human subjects. The method is not limited to treating obesity in non-diabetic obese human patients, but encompasses treating obesity in type II diabetic human patients, 80-90% of whom are known in the art to have intrinsic obesity. In other words, treatment of obesity in type II diabetic human patients is just one of the species or embodiments encompassed within the scope of the genus of human subjects in need of such treatment. That 10-20% of the prior art diabetic patients, to whom pramlintide is administered, are not expected to be obese is not relevant since an anticipatory reference has to teach only one species or one embodiment encompassed by the scope of the genus claims. Under the principles of inherency, a reference may be directed to an entirely different problem than the one addressed by the inventor, or may be from an entirely different field of endeavor than that of the claimed invention, yet the reference is still anticipatory if it explicitly or inherently discloses every limitation recited in the claims. See *State Contracting & Eng'g Corp. v. Condotte America, Inc.*, 346 F.3d 1057, 1068, 68 USPQ2d 1481, 1488 (Fed. Cir. 2003). Appellants appear to be arguing that in order to be anticipatory, a prior art reference has to teach each and every species or embodiment encompassed within the scope of the claims. The argument is not persuasive.

For the reasons delineated above, the art rejection should be sustained.

(IV) In response to the rejection of claims 7, 14, 16 and 17 made in paragraph 35 of the Office Action mailed 02/11/08 and maintained in paragraph 17 of the Office Action mailed 04/30/08 under 35 U.S.C § 102(b) over Kolterman *et al.* (*Diabetologia* 39: 492-499, April, 1996) (Kolterman *et al.*, 1996) as evidenced by Itasaka *et al.* (*Psychiatr. Clin. Neurosci.* 54: 340-341, June 2000), Appellants submit the following arguments.

(a) Kolterman 1996 merely describes the use of an amylin agonist, pramlintide, for treating patients with insulin-dependent diabetes mellitus and demonstrates *inter alia* that administration of the amylin agonist significantly reduces postprandial plasma glucose concentrations. Kolterman 1996 discloses neither the use of the amylin agonist for treating obesity nor a reduction in body weight in those patients administered the amylin agonist. Kolterman 1996 does not report the weight of the subjects at the end of the study and nothing in the reference indicates that pramlintide had any effect on the weight of the subjects. Kolterman 1996 is silent with regard to the effect of the amylin agonist on body weight. In an effort to cure the deficiencies of Kolterman 1996, the Examiner relies on Itasaka to allegedly provide a correlation between body mass index (BMI) and obesity. However, nothing in Kolterman 1996 (with or without evidence of Itasaka) suggests that an amylin agonist can be useful in the treatment of obesity, or in the selection of a subject population for such method of treatment. The patient population of Kolterman 1996 is not necessarily the same as the claimed subject, *i.e.,* a subject in need of treatment for obesity.

(b) The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert, 9* F.3d 1531, 1534 (Fed. Cir. 1993). "To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the references, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson* 169 F.3d 743,745 (Fed. Cir. 1999).

Appellants' arguments have been carefully considered, but are not persuasive. Clearly, the Office has set forth a *prima facie* case of anticipation.

Contrary to Appellants' assertion, the prior art method necessarily includes *all* of the elements of the instant claims. As set forth previously, Kolterman *et al.* (1996) taught a method of subcutaneous administration of 30, 100, or 300 μg of pramlintide composition or AC137 (i.e., $^{25, 28,}$ ^{29}pro-h-amylin), a human amylin analogue, to human patients with insulin-dependent diabetes mellitus or IDDM who are on insulin. Pramlintide is administered three times daily for a period of 14 days. See abstract; and page 493. The mean body weight ± SEM of diabetic patients included in Kolterman's (1996) method who were administered subcutaneously with 30 micrograms, 100

micrograms, and 300 micrograms of pramlintide, three times a day for 14 days, was 70.6 $\pm$ 2.7, 74.4 $\pm$ 2.5, and 75.7 $\pm$ 2.6 respectively, a body weight similar to the 70 kg body weight of the human patient disclosed at lines 4-8 of page 23 of the substitute instant specification; and paragraph bridging pages 23 and 24 and lines 3-7 on page 24 of Appellants' response filed December 2002. Note that the human patient in need of the recited treatment according to the instant invention is expressly identified in the instant specification as one having a body weight of 79 kg. For example, the recited therapeutic amount range of 'about 0.1 milligrams per day to about 1 milligram per day', or 'about 0.01 to about 5 mg/day', or 0.03 to about 5 mg/day of the amylin agonist or amylin agonist analogue, pramlintide, administered is specifically "for a 70 kg patient". See lines 4-8 of page 23 of the substitute instant specification; and paragraph bridging pages 23 and 24 and lines 3-7 on page 24 of Appellants' response filed December 2002. Therefore, the 70.6 to 75.7 kg diabetic patients from Kolterman's (1996) study qualify as 'human subjects in need thereof' as recited in the instant claims. Additionally, even body mass index (BMI)-wise, Kolterman's (1996) diabetic subjects meet the limitation 'human subjects in need of treatment of obesity' as recited in the instant claims, because the diabetic subjects included in Kolterman's method (1996) had a BMI of up to 27. See second full paragraph under 'Subjects, materials and methods'. Therefore, Kolterman's (1996) diabetic subjects having a BMI at least in the range of 24 up to 27 do qualify as obese diabetic subjects in light of what is known in the art. For example, Itasaka *et al.* teach that a BMI of 24.0 to 26.4 represents mild obesity and 26.4 and heavier (i.e., including a BMI of 26.4 to 27) represents obesity in humans (see abstract of Itasaka *et al.*). Note that Kolterman's (1996) pramlintide composition did not comprise another obesity relief agent, but consisted of or consisted essentially of pramlintide. The pramlintide composition was injected subcutaneously to the diabetic human patients (see the section 'Study design') and therefore is expected to inherently contain a pharmaceutically acceptable carrier therein. The amount administered was 30 micrograms three times a day to 'about 0.1 milligrams' or 300 micrograms per day. See the section 'Study design'; Table 1; and paragraph therebelow. Clearly, Kolterman's (1996) subcutaneous administration of a therapeutically effective amount of the amylin agonist ^{25,28,29}Pro-human amylin to diabetic human subjects weighing 70 kg or more, or having a BMI falling in the BMI range of 24 up to 27 anticipates the instant claims. Thus, the very active step recited in the instantly claimed method was disclosed and practiced by Kolterman *et al.* in April, 1996. The prior art method of administering the above-explained amount of the amylin agonist ^{25,28,29}Pro-human amylin (pramlintide or SEQ ID

NO: 1) to diabetic human subjects weighing 70 kg or more, and/or having a BMI falling in the range of 24 up to 27 necessarily serves as the Appellants' method. Given that the method step in Kolterman's (1996) method and the instant claims are the *same* and the amount of pramlintide administered are the *same*, Kolterman's (1996) method is expected to necessarily bring about the same therapeutic effect in the pramlintide-treated diabetic patients as defined in the instant invention, i.e., by controlling body weight for cosmetic purposes, or by improving bodily appearance in the diabetic patients, or by inhibiting weight gain. That the determination of inherency in the instant case is certainly not established by probabilities or possibilities is further evidenced by the teachings of Rattner *et al.* (*Exp. Clin. Endocrinol. Diabetes* 113: 199-204, 2005) (Rattner *et al.* 2005). The reference of Rattner *et al.* (2005) is set forth herein solely to address Appellants' arguments. The reference of Rattner *et al.* (2005), which is co-authored by the inventor OG Kolterman, show that subcutaneous administration of 30 or 60 micrograms of TID or QID pramlintide to insulin-taking IDDM patients having a body weight of 76.0 ± 14.3 kg or a BMI of > 25 kg/m^2, concurrently induced *a significant decline in weight*. See sections 'Subjects and Methods'; Results; Table 1; and Figure 1B of Rattner *et al.* (2005). Therefore, Kolterman's (1996) method necessarily served as a method of treating obesity. It is particularly noted that Appellants have advanced no arguments with regard to the teachings of Rattner *et al.* (2005), the reference that was cited to show that the missing inherent matter is necessarily present in the method thing described in the prior art reference of Kolterman *et al.* (1996).

In sum, since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist pramlintide administered in the claimed method are merely inherent and do not necessarily make the claimed method patentable. *Ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993) (The Board rejected a claim directed to a method for protecting a plant from plant pathogenic nematodes by inoculating the plant with a nematode inhibiting strain of *P. cepacia*. A U.S. patent to Dart disclosed inoculation using *P. cepacia* type Wisconsin 526 bacteria for protecting the plant from fungal disease. Dart was silent as to nematode inhibition but the Board concluded that nematode inhibition was an inherent property of the bacteria. The Board noted that applicant had stated in the specification that Wisconsin 526 possesses an 18% nematode inhibition rating.). In the instant application, the obesity-relief or weight loss-induction is an inherent property inseparable from the administered pramlintide. Since the structural

limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the disclosure of Kolterman *et al.* ('1996), Kolterman's ('1996) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the weight gain-inhibiting effect, weight loss-inducing effect, or obesity-treating effect. The two structurally identical pramlintide compounds administered in the two methods (i.e., the prior art method and the instant method) cannot have mutually exclusive properties. The same two methods cannot have mutually exclusive results.

'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Itasaka's extrinsic evidence makes clear that the missing descriptive matter, i.e., a BMI of 24.0 to 26.4 as present in Kolterman's diabetic patients represents mild obesity and a BMI of 26.4 and heavier as present in Kolterman's diabetic patients (i.e., including a BMI of 26.4 to 27) represents obesity in humans, and therefore is necessarily present in the method thing described by Kolterman *et al.* (1996). The method of Kolterman *et al.* (1996) clearly anticipates the claimed method of the instant invention, because Kolterman *et al.* (1996) taught the very step of the instantly claimed method in human IDDM patients. The alleged failure of Kolterman *et al.* (1996) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Kolterman *et al.* (1996). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

'A generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus'. The species in that case will anticipate the genus. *In re Slayter*, 276 F.2d 408,

411, 125 USPQ 345, 347 (CCPA 1960); *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989). A genus does not always anticipate a claim to a species within the genus. However, when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. In *In re Sivaramakrishnan*, 673 F.2d 1383, 213 USPQ 441 (CCPA 1982), the claims were directed to polycarbonate containing cadmium laurate as an additive. The court upheld the Board's finding that a reference specifically naming cadmium laurate as an additive amongst a list of many suitable salts in polycarbonate resin anticipated the claims. The applicant had argued that cadmium laurate was only disclosed as representative of the salts and was expected to have the same properties as the other salts listed while, as shown in the application, *cadmium laurate had unexpected properties*. The court held that it *did not matter that the salt was not disclosed as being preferred, the reference still anticipated the claims* and because the claim was anticipated, *the unexpected properties were immaterial*. Although the instant claims are method claims, in the instant application, the prior art disclosure of a method comprising or consisting of the subcutaneous administration of 30 micrograms, 100 micrograms, and 300 micrograms of pramlintide, three times a day for 14 days of the amylin agonist, ^{25,28,29}Pro-human amylin, to the human diabetic patient species weighing 70 kg or more, and/or having a BMI falling in the range of 24 up to 27 anticipates the instantly claimed method which uses generic human subjects in need of treatment of obesity. The claims are anticipated because the administered ^{25,28,29}Pro-human amylin also inherently exerted obesity-relieving properties in said method. See also *Ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993) (The Board rejected a claim directed to a method for protecting a plant from plant pathogenic nematodes by inoculating the plant with a nematode inhibiting strain of *P. cepacia*. A U.S. patent to Dart disclosed inoculation using *P. cepacia* type Wisconsin 526 bacteria for protecting the plant from fungal disease. Dart was silent as to nematode inhibition but the Board concluded that nematode inhibition was an inherent property of the bacteria. The Board noted that applicant had stated in the specification that Wisconsin 526 possesses an 18% nematode inhibition rating.). In the instant application, the obesity-relief or weight loss-induction is an intrinsic property inseparable from the administered pramlintide. The two structurally identical pramlintide compounds administered in the two methods (i.e., the prior art method and the instant method) cannot have mutually exclusive properties. As set forth above, this is evidenced by the teachings of Rattner *et al.* (2005), which is co-authored by the inventor OG Kolterman.

In the instant case, the claims are drawn to a method that uses generic human subjects in need of treatment of obesity. The generic limitation 'human subject' in the instant claims does not exclude 'a 70 kg patient'. The method is not limited to treating obesity in non-diabetic obese human patients, but encompasses treating obesity in type I diabetic human patients weighing 70 kg or more, and/or having a BMI falling in the range of 24 up to 27. In other words, treatment of obesity in type I diabetic human patients is just one of the species or embodiments encompassed within the scope of the genus of human subjects in need of such treatment. An anticipatory reference has to teach only one species or one embodiment encompassed by the scope of the genus claims. Furthermore, under the principles of inherency, a reference may be directed to an entirely different problem than the one addressed by the inventor, or may be from an entirely different field of endeavor than that of the claimed invention, yet the reference is still anticipatory if it explicitly or inherently discloses every limitation recited in the claims. See *State Contracting & Eng'g Corp. v. Condotte America, Inc.*, 346 F.3d 1057, 1068, 68 USPQ2d 1481, 1488 (Fed. Cir. 2003). Appellants appear to be arguing that in order to be anticipatory, a prior art reference has to teach each and every species or embodiment encompassed within the scope of the claims. The argument is not persuasive.

For the reasons delineated above, the art rejection should be sustained.

(V) In response to the rejection of claims 7, 14, 16 and 17 made in paragraph 26 of the Office Action mailed 02/11/08 and maintained in paragraph 11 of the Office Action mailed 04/30/08 under the judicially created doctrine of obviousness-type double patenting over claims 34 and 35 of Gaeta *et al.* ('411) as evidenced by Tsanev, Appellants submit the following arguments.

(a) The alleged prior art does not include all of the elements of the instant claims as required by the law. The references provide no guidance concerning the identification of or intent to treat a subject in need of treatment for obesity. The predecessor court to the Federal Circuit held that the inherency of an advantage and its obviousness are entirely different questions, that which may be inherent is not necessarily known, and that obviousness cannot be predicated on what is unknown.

(b) Claims 7, 14, 16 and 17 are directed to methods for treating obesity in a human subject in need of such treatment, which methods require administration of a composition or compound containing an amylin or an amylin agonist, wherein the amount of the composition or compound administered is effective to treat obesity by inhibiting weight gain or inducing weight loss, and wherein

the subject is in need of treatment for obesity. Claims 34 and 35 of Gaeta are merely directed to methods for the treatment of diabetes mellitus in a mammal comprising the administration of a therapeutically effective amount of a particular amylin agonist analogue. Gaeta is silent with respect to the treatment of obesity.

(c) In an attempt to cure the deficiency of claims 34 and 35 of Gaeta, the Office relies on Tsanev to assert that 80-90% of diabetic patients are obese. Even in view of Tsanev, a claim to treating diabetes mellitus with an amylin agonist analogue (i.e., claims of Gaeta) does not teach or suggest treating subjects as currently claimed. Nothing in the cited claims teaches or suggests the identification of or intent to treat a subject in need of treatment for obesity. The courts have held that the phrase 'in need thereof' as recited in independent claims 7, 14 and 16 is meaningful, and that 'the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose." *Jansen v. RexallSundown, Inc.* 342 F.3d 1329, 1333 (Fed. Cir. 2003). Since the cited claims do not teach or suggest treating obesity, the intent to treat human subjects in need of treatment for obesity, or the use of an amount effective to treat obesity, a skilled artisan would have no expectation of success for the claimed invention in view of the cited claims. In this regard, "[r]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR,* 127 S.Ct. at 1741 (quoting *In re Kahn* 441 F.3d 977, 988 (Fed. Cir. 2006). The prior art must still suggest a predictable outcome to establish a *prima facie* case of obviousness. See, e.g., *Takeda Chemical Industries, LM v. Alphapharm Pry., Ltd.* 492 F.3d 1350, 83 U.S.P.Q.2d 1169 (Fed. Cir. 2007).

(d) The disclosure of Gaeta, whether evidenced by Tsanev or not, is silent with respect to the treatment of obesity. Gaeta did not disclose that an amylin or amylin agonist is useful for treating obesity in a human in need of treatment thereof. The Office's reliance on inherency in the context of anticipation in the rejection(s) is contrary to the law. Anticipation based on inherency is appropriate only when the prior art relied upon necessarily includes all of the elements of the claims in question and is the natural result of following the instructions or examples of the prior art. See, *Atofina v. GreatLakes Chemical Corp.,* 441 F.3d 991, 78 USPQ2d 1417, 1424 (Fed. Cir. 2006); *SmithKline Beecham Corp. v. Apotex Corp.,* 403 F.3d 1331, 1334, 74 USPQ2d 1398, 1407 (Fed. Cir. 2005) (citing

Schering Corp. v. Geneva Pharms., Inc., 339 F. 3d 1373, 1377, 67 USPQ2d 1664, 1667 (Fed. Cir. 2003)). The Court in *Schering* relied in part on the decision *In re Cruciferous Sprouts Litigation,* 301 F.3 d 1343, 1351, 64 USPQ2d 1202, 1206 (Fed. Cir. 2002) wherein it was noted that to demonstrate inherency, it was necessary to show that the prior art necessarily, always functions in accordance with the claims addressed. The requirement that the teaching of a reference always, under any circumstances, necessarily satisfies the recitation of the claims to make out a case of inherent anticipation was reaffirmed by the Federal Circuit in *Abbott Laboratories v. Baxter Pharmaceutical Products, Inc.,* 471 F.3d 1363, 1368 (Fed. Cir. 2006). It is well settled that a determination of inherency cannot be established by probabilities or possibilities, but that it is incumbent upon the Examiner to establish the inevitability of the inherency which is propounded. *In re Oelrich,* 666 F.2d 578, 581,212 USPQ 323,326 (CCPA 1981); *In re Wilding,* 535 F.2d 631, 635-36, 190 USPQ 59, 63-64 (CCPA 1976). Tsanev discloses that 80-90% of diabetic patients are obese, which falls short of the 100% (i.e., always, under any circumstances) criterion required by the present claims and required by the law. Accordingly, claims 34 and 35 of Gaeta support neither *prima facie* obviousness nor anticipation with regard to the claimed invention.

(e) The Office improperly asserts that the prior method necessarily includes all of the elements of the instant claims as evidenced by Thompson *et al.* (*Diabetes* 46: Suppl. 1, page 30A, 0116, 02 May 1997) (Thompson 1997). Appellants had filed a declaration under 37 C.F.R. § 1.131 in the response to Office Action filed December 2, 2002, which demonstrates that the current application antedates Thompson 1997 and was inventors' own work. Accordingly, Thompson 1997 is unavailable as prior art against the current application. More particularly, Thompson 1997 cannot be used as evidence of an alleged inherency because the present invention antedates Thompson 1997. See *In re Shetty (Id.).* Thus, the Office has failed to provide evidence or argument with any rational underpinning that the current claims are obvious in view of Gaeta as evidenced by Tsanev. Whatever else is taught by Gaeta and Tsanev, the references do not teach or suggest a method of treating obesity in a subject in need of treatment thereof.

The Office submits the following rebuttal to Appellants' arguments:

Contrary to Applicants' assertion, the prior art method necessarily includes *all* of the elements of the instant claims. As set forth previously, the '411 patent's patients seen by a medical practitioner, i.e., humans having diabetes mellitus, was administered with a therapeutically effective amount of the

amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (SEQ ID NO: 1 or pramlintide), the same amylin agonist analogue recited in instant claim 17. The method of treatment claimed in claims 34 and 35 of the '411 patent includes administering to such a patient with diabetes mellitus a therapeutically effective amount of the amylin agonist of claim 19 of the '411 patent, ^{25,28,29}Pro-human amylin (SEQ ID NO: 1 or pramlintide). The portion of the disclosure of the '411 patent at second paragraph under 'Summary of the Invention' supporting the limitations 'diabetes mellitus' and 'administration of …. an amylin agonist analogue' include insulin-requiring diabetes mellitus and administration of an amylin agonist analogue alone (i.e., consisting of) or in conjunction with (comprising or consisting essentially of) insulin or a glucagon, i.e., not in conjunction with another obesity relief agent. The portion of the disclosure of the '411 patent at lines 53-59 in column 8 supporting the limitation 'therapeutically effective amount' of the amylin agonist includes the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. The amount effective to inhibit weight gain or induce weight loss, i.e., treat obesity, encompassed in the instant claims as described in the instant application of about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, about 0.1 milligrams to about 1 milligram per day, or 300 micrograms per dose, falls within the range disclosed in the '411 patent. Given the art-known prevalence of intrinsic obesity in as many as 80% to 90% of diabetic patients as disclosed by Tsanev, 80-90% of the human diabetic patients used in the method disclosed in the '411 patent qualified as human patients in need of treatment for obesity. Therefore, the method of the '411 patent comprising or consisting of the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist, ^{25,28,29}Pro-human amylin alone or in conjunction with insulin or glucagon, to 80-90% of the human diabetic patients anticipates the instant claims. Given that the method step of the '411 patent and the instant claims are the same, the amylin agonist analogue pramlintide used and its amount administered are the same, and the human diabetic patients used are the same (80-90% of whom are known to be obese), the method of the '411 patent is expected to necessarily bring about a weight gain-inhibiting effect, weight loss-inducing effect, or obesity-treating effect in the intrinsically obese diabetic patient administered with a therapeutically effective amount of the pramlintide as claimed in the instant invention. Since the structural limitations of the instantly claimed method and *all* of the criteria required by the instant claims are met by the disclosure of Gaeta *et al.* ('411), Gaeta's ('411) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the weight gain inhibiting effect, weight loss-inducing effect, or obesity-treating effect.

That the determination of inherency in the instant case is not established by probabilities or possibilities is further evidenced by the teachings of Thompson *et al.* (*Diabetes* 46: Suppl. 1, page 30A, 0116, 02 May 1997) (Thompson *et al.* May, 1997). The reference of Thompson *et al.* is cited solely to rebut Appellants' arguments by showing that the missing inherent matter is necessarily present in the method thing described in the prior art reference of '411 patent. Thompson *et al.* (May, 1997) showed that a method of subcutaneous administration of pramlintide, i.e., $^{25, 28, 29}$pro-h-amylin, an analog of human amylin, i.e., the same amylin agonist used in the instant invention, to patients with type II diabetes requiring insulin, at a dose 60 micrograms QID (i.e., four times a day) or TID (i.e., three times a day) not only improved glycemic control in these patients, ***but also decreased body weight*** concurrently (see abstract). Therefore, the method of the '411 patent necessarily served as a method of treating obesity. With regard Appellants' statement that Thompson (1997) cannot be used as evidence of an alleged inherency because the present invention antedates Thompson 1997, it should be noted that the critical date of extrinsic evidence need *not* antedate the filing date of the instant application. See MPEP § 2124.

It is a commonly known fact in the art that type II diabetic patients (80-90% of whom are known to be obese) are 'in need of' obesity. Appellants themselves characterize Type 2 diabetic subjects taking insulin as a particularly difficult to treat obese subject population. See top of page 14 of Appellants' after-final amendment. With regard to the Appellants' statement that Tsanev's disclosure that 80-90% of diabetic patients are obese falls short of the 100% (i.e., always, under any circumstances), the following must be noted. 'A generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus'. The species in that case will anticipate the genus. *In re Slayter*, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989). A genus does not always anticipate a claim to a species within the genus. However, when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named. In *In re Sivaramakrishnan*, 673 F.2d 1383, 213 USPQ 441 (CCPA 1982), the claims were directed to polycarbonate containing cadmium laurate as an additive. The court upheld the Board's finding that a reference specifically naming cadmium laurate as an additive amongst a list of many suitable salts in polycarbonate resin anticipated the claims. The applicant had argued that cadmium laurate was only disclosed as representative of the salts and was expected to have the same properties as the other salts listed while, as shown in the application, *cadmium laurate had unexpected properties*. The court held that it *did not matter that the salt was not disclosed as being preferred, the reference still*

anticipated the claims and because the claim was anticipated, *the unexpected properties were immaterial*. Although the instant claims are method claims, in the instant application, the prior art disclosure of a method comprising or consisting of the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist, ^{25,28,29}Pro-human amylin alone or in conjunction with insulin or glucagon, to 80-90% of the human diabetic patients anticipates the instantly claimed method. The claims are anticipated because the administered ^{25,28,29}Pro-human amylin also inherently exerted obesity-relieving properties in said method. See also *Ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993) (The Board rejected a claim directed to a method for protecting a plant from plant pathogenic nematodes by inoculating the plant with a nematode inhibiting strain of *P. cepacia*. A U.S. patent to Dart disclosed inoculation using *P. cepacia* type Wisconsin 526 bacteria for protecting the plant from fungal disease. Dart was silent as to nematode inhibition but the Board concluded that nematode inhibition was an inherent property of the bacteria. The Board noted that applicant had stated in the specification that Wisconsin 526 possesses an 18% nematode inhibition rating.). In the instant application, the obesity-relief or weight loss-induction is an intrinsic property inseparable from the administered pramlintide. The two structurally identical pramlintide compounds administered in the two methods (i.e., the prior art method and the instant method) cannot have mutually exclusive properties. As set forth above, this is evidenced by the teachings of Thompson *et al*. (1997) who showed that a method of subcutaneous administration of pramlintide, i.e., $^{25, 28, 29}$pro-h-amylin, an analog of human amylin, i.e., an amylin agonist, to patients with type II diabetes requiring insulin, at a dose 60 micrograms QID or TID not only improved glycaemic control in these patients, but also decreased body weight concurrently (see abstract). Therefore, the prior art method necessarily served as a method of treating obesity. The same two methods (i.e., the prior art method and the instant method) cannot have mutually exclusive results.

In the instant application, it is important to note that the *human patients used in the instant specification for treatment of obesity via administration of pramlintide are indeed type II diabetic human patients*. Thus, the prior art disclosure is commensurate in scope with the instant disclosure with regard to the type 2 diabetic human subject population used, the pramlintide compound administered, the amount and frequency of pramlintide administered, to the type 2 diabetic human patient species.

In the instant case, the claims are drawn to a method that uses generic human subjects. The method is not limited to treating obesity in non-diabetic obese human patients, but encompasses treating obesity in type II diabetic human patients, 80-90% of whom are known in the art to have intrinsic

obesity. In other words, treatment of obesity in type II diabetic human patients is just one of the species or embodiments encompassed within the scope of the genus of human subjects in need of such treatment. That 10-20% of prior art diabetic patients, to whom pramlintide is administered, are not expected to be obese is not relevant since an anticipatory reference has to teach only one species or one embodiment encompassed by the scope of the genus claims. Under the principles of inherency, a reference may be directed to an entirely different problem than the one addressed by the inventor, or may be from an entirely different field of endeavor than that of the claimed invention, yet the reference is still anticipatory if it explicitly or inherently discloses every limitation recited in the claims. See *State Contracting & Eng'g Corp. v. Condotte America, Inc.*, 346 F.3d 1057, 1068, 68 USPQ2d 1481, 1488 (Fed. Cir. 2003). Appellants appear to be arguing that in order to be anticipatory, a prior art reference has to teach each and every species or embodiment encompassed within the scope of the instant claims. The argument is not persuasive.

For the reasons delineated above, the rejection should be sustained.

(VI) In response to the rejection of claims 7, 14 and 16 made in paragraph 27 of the Office Action mailed 02/11/08 and maintained in paragraph 12 of the Office Action mailed 04/30/08 under the judicially created doctrine of obviousness-type double patenting over claims 11 and 13 of Beumont *et al.* ('008) as evidenced by Tsanev, Appellants submit the following argument.

In view of the similarity of the current rejection to the double patenting rejection over Gaeta discussed above, arguments provided above in relation to that rejection are reiterated. Arguments provided for the double patenting rejection over Gaeta ('411) are hereby reiterated. Appellants are referred to section V above for the Office's response.

(VII) In response to the rejection of claims 7, 14 and 16 made in paragraph 34 of the Office Action mailed 02/11/08 and maintained in paragraph 16 of the Office Action mailed 04/30/08 under 35 U.S.C § 102(e)(2) over Beumont *et al.* ('008) as evidenced by Tsanev, Appellants reiterate the same arguments that they have presented on the obviousness double patenting rejection over US patent 5,321,008. Appellants are referred to sections V and VI above for the Office's response.

'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make

clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in 80 to 90% of Beumont's ('008) insulin-requiring diabetic subjects administered with calcitonin, is necessarily present in the method thing described by Beumont *et al.* ('008). The method of Beumont *et al.* ('008) clearly anticipates the claimed method of the instant invention, because Beumont *et al.* ('008) taught the very step of the instantly claimed method in the very same diabetic human patient. The alleged failure of Beumont *et al.* ('008) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Beumont *et al.* ('008). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

For the reasons delineated above, the rejection should be sustained.

(VIII) In response to the rejection of claims 7, 14, 16 and 17 made in paragraph 35 of the Office Action mailed 02/11/08 and maintained in paragraph 17 of the Office Action mailed 04/30/08 under 35 U.S.C § 102(e)(2) over Gaeta *et al.* ('411) as evidenced by Tsanev, Appellants reiterate the same arguments that they have presented on the obviousness double patenting rejection over US patent 5,686,411. Appellants are referred to section V above for the Office's response.

To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of

record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in at least one of Gaeta's ('411) insulin-requiring diabetic subjects administered with ^{25,28,29}Pro-human amylin, is necessarily present in the thing described by Gaeta *et al.* ('411). The method of Gaeta *et al.* ('411) clearly anticipates the claimed method of the instant invention, because Gaeta *et al.* ('411) taught the very step of the instantly claimed method in the very same diabetic human patient species. The alleged failure of Gaeta *et al.* ('411) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Gaeta *et al.* ('411). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See *Mehl/Biophile International Corp. v. Milgraum*, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing *W.L. Gore & Assocs. v. Garlack, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

For the detailed reasons delineated above, the rejections of record should be sustained.

(11) Related Proceedings Appendix

No decision rendered by a court or the Board is identified by the Examiner in the Related Appeals and Interferences section of this examiner's answer.

Respectfully submitted,

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